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                 The retention policy for unread STNmail messages
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                 will change in 2009 for STN-Columbus and STN-Tokyo
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         JAN 07
                 WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
                 Classification Data
NEWS
         FEB 02
                 Simultaneous left and right truncation (SLART) added
                 for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS
         FEB 02
                 GENBANK enhanced with SET PLURALS and SET SPELLING
      7
                 Patent sequence location (PSL) data added to USGENE
NEWS
         FEB 06
         FEB 10
                 COMPENDEX reloaded and enhanced
NEWS
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         FEB 11
                 WTEXTILES reloaded and enhanced
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                 patent records provide insights into related prior
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         FEB 23
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         FEB 23
                 TOXCENTER updates mirror those of MEDLINE - more
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                 precise author group fields and 2009 MeSH terms
         FEB 23
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NEWS 15
                 STN patent clusters
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         FEB 25
                 USGENE enhanced with patent family and legal status
                 display data from INPADOCDB
NEWS 17
         MAR 06
                 INPADOCDB and INPAFAMDB enhanced with new display
                 formats
NEWS 18
                 EPFULL backfile enhanced with additional full-text
         MAR 11
                 applications and grants
                 ESBIOBASE reloaded and enhanced
NEWS 19
         MAR 11
NEWS 20
         MAR 20
                 CAS databases on STN enhanced with new super role
                 for nanomaterial substances
NEWS 21
         MAR 23
                 CA/CAplus enhanced with more than 250,000 patent
                 equivalents from China
NEWS 22
         MAR 30
                 IMSPATENTS reloaded and enhanced
NEWS 23
                 CAS coverage of exemplified prophetic substances
         APR 03
                 enhanced
NEWS 24
         APR 07
                 STN is raising the limits on saved answers
NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
             AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.
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=> fil reg
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FULL ESTIMATED COST

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STRUCTURE FILE UPDATES: 23 APR 2009 HIGHEST RN 1138395-00-2 DICTIONARY FILE UPDATES: 23 APR 2009 HIGHEST RN 1138395-00-2

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ring nodes :
1 \quad \overset{.}{2} \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \quad 8 \quad 9 \quad 10 \quad 12 \quad 13 \quad 14 \quad 15 \quad 16 \quad 17 \quad 19 \quad 20 \quad 21 \quad 22 \quad 23
ring/chain nodes :
18
chain bonds :
7-18 9-12 18-19
ring bonds :
1-2 \quad 1-6 \quad 2-3 \quad 3-4 \quad 4-5 \quad 5-6 \quad 5-7 \quad 6-10 \quad 7-8 \quad 8-9 \quad 9-10 \quad 12-13 \quad 12-17 \quad 13-14 \quad 14-15
15-16 16-17 19-20 19-23 20-21 21-22 22-23
exact/norm bonds :
7-18 18-19 19-20 19-23 20-21 21-22 22-23
exact bonds :
9 - 12
normalized bonds :
1-2 \quad 1-6 \quad 2-3 \quad 3-4 \quad 4-5 \quad 5-6 \quad 5-7 \quad 6-10 \quad 7-8 \quad 8-9 \quad 9-10 \quad 12-13 \quad 12-17 \quad 13-14 \quad 14-15
15-16 16-17
isolated ring systems :
containing 1 : 12 :
Match level:
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1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom

L1 STRUCTURE UPLOADED

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Structure attributes must be viewed using STN Express query preparation.

=> s 11 SAMPLE SEARCH INITIATED 17:38:14 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 38 TO ITERATE

100.0% PROCESSED 38 ITERATIONS 3 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 391 TO 1129
PROJECTED ANSWERS: 3 TO 162

L2 3 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 17:38:18 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 815 TO ITERATE

100.0% PROCESSED 815 ITERATIONS 59 ANSWERS

SEARCH TIME: 00.00.01

L3 59 SEA SSS FUL L1

=> d scan

L3 59 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN Ethanone, 1-[2,3-dihydro-5-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-1H-indol-1-yl]-

MF C23 H19 N5 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L3 59 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 1H-Inden-2-ol, 2,3-dihydro-1-[[7-methyl-2-(4-pyridinyl)-4quinazolinyl]amino]-, (1S,2R)-

MF C23 H20 N4 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 59 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 2-Naphthalenol, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-

MF C23 H16 N4 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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COST IN U.S. DOLLARS SINCE FILE TOTAL

ENTRY SESSION

FULL ESTIMATED COST 188.28 188.50

FILE 'CAPLUS' ENTERED AT 17:38:43 ON 24 APR 2009
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FILE 'REGISTRY' ENTERED AT 17:35:21 ON 24 APR 2009 STRUCTURE UPLOADED L13 S L1 L2L3 59 S L1 SSS FULL FILE 'CAPLUS' ENTERED AT 17:38:43 ON 24 APR 2009 => s 1315 L3 L4=> s 15 and (pry<2004) L5 NOT FOUND The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>). => s 14 and (pry<2004)4270617 PRY<2004 12 L4 AND (PRY<2004) 1.5

=> s 1-12 ibib abs hitstr 10110032 1 1630991 12 16 IBIB 250982 ABS 4 ABSES 250986 ABS (ABS OR ABSES) L6 0 1-12 IBIB ABS HITSTR (1(W)12(W)IBIB(W)ABS(W)HITSTR)=> d 15 1-12 ibib abs hitstr ANSWER 1 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN L5

ACCESSION NUMBER: 2004:902403 CAPLUS

DOCUMENT NUMBER: 141:374752

TITLE: Heterocyclic compound modulators of kinases,

particularly Tie-2 kinase, and use in the treatment of

kinase-dependent diseases

INVENTOR(S): Ibrahim, Mohamed; Leahy, James; Sangalang, Joan C.; Schnepp, Kevin; Shi, Xian; Nuss, John

PATENT ASSIGNEE(S): Exelixis, Inc., USA SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO	2004	0921	96		A2 20041028 A3 20050317												
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		SK, TD,	•	BF,	ВЈ,	CF,	CG,	C1,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝĿ,	SN,
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	2520																408 <
EP	1610														_		408 <
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US	2007	0161	651		A1		2007	0712		US 2	005-	5524	26		2	0051	007 <
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PIIDD O	STIDOR	101			MADI		1 11 .	2747	E 0								

OTHER SOURCE(S): MARPAT 141:374752

AB The invention provides compds. for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. Compds. of the invention inhibit, regulate and/or modulate kinases, particularly Tie-2. Methods of using the compds. and pharmaceutical compns. thereof to treat kinase-dependent diseases and conditions are also an aspect of the invention. Preparation of quinazoline compds. of the invention is described.

TT 332850-36-9P 781615-21-2P 781615-27-8P 781615-29-0P 781615-32-5P 781615-35-8P 781615-39-2P 781615-40-5P 781615-41-6P 781615-42-7P 781615-59-6P 781615-60-9P 781615-61-0P 781615-64-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(heterocyclic compound modulators of kinases, particularly Tie-2 kinase, and use in treatment of kinase-dependent diseases)

RN 332850-36-9 CAPLUS

CN 4-Quinazolinamine, N-cyclohexyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-21-2 CAPLUS

CN 4-Quinazolinamine, N-cyclopentyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-27-8 CAPLUS

CN 4-Quinazolinamine, N-(2,3-dihydro-1H-inden-1-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-29-0 CAPLUS

CN 4-Quinazolinamine, 2-(4-pyridinyl)-N-[(2R)-1,2,3,4-tetrahydro-2-naphthalenyl]- (CA INDEX NAME)

RN 781615-32-5 CAPLUS

CN 4-Quinazolinamine, 2-(4-pyridinyl)-N-[(2S)-1,2,3,4-tetrahydro-2-naphthalenyl]- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-35-8 CAPLUS

CN 1H-Inden-2-ol, 2,3-dihydro-1-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, (1S,2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-39-2 CAPLUS

CN 4-Quinazolinamine, N-[(1S,2S)-2-(phenylmethoxy)cyclopentyl]-2-(4-pyridinyl)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-40-5 CAPLUS

CN 1,4-Benzenediamine, N1-phenyl-N4-[2-(4-pyridinyl)-4-quinazolinyl]- (CA INDEX NAME)

RN 781615-41-6 CAPLUS

CN 2-Naphthalenol, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 781615-42-7 CAPLUS

CN 4-Quinazolinamine, N-[4-(1-methylethoxy)phenyl]-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-59-6 CAPLUS

CN 1H-Inden-2-ol, 1-[[2-(2-ethyl-4-pyridinyl)-4-quinazolinyl]amino]-2,3-dihydro-, (1S,2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-60-9 CAPLUS

CN 1H-Inden-2-ol, 1-[[2-(2-ethyl-4-pyridinyl)-4-quinazolinyl]amino]-2,3-dihydro-, (1R,2S)- (CA INDEX NAME)

RN 781615-61-0 CAPLUS

CN 1H-Inden-2-ol, 1-[[6-bromo-2-(4-pyridinyl)-4-quinazolinyl]amino]-2,3-dihydro-, (1S,2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-64-3 CAPLUS

CN 1H-Inden-2-ol, 2,3-dihydro-1-[[2-(4-pyridinyl)-7-(trifluoromethyl)-4-quinazolinyl]amino]-, (1S,2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-67-6 CAPLUS
CN 1H-Inden-2-ol, 2,3-dihydro-1-[[7-methyl-2-(4-pyridinyl)-4-quinazolinyl]amino]-, (1S,2R)- (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS 4 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:534191 CAPLUS

DOCUMENT NUMBER: 141:89100

TITLE: Preparation of (quinazolin-4-yl)amines as capsaicin

receptor modulators

INVENTOR(S):

Bakthavatchalam, Rajagopal; Blum, Charles A.; Brielmann, Harry; Caldwell, Timothy M.; De Lombaert,

Stephane; Hodgetts, Kevin J.; Zheng, Xiaozhang

Neurogen Corporation, USA PATENT ASSIGNEE(S):

PCT Int. Appl., 226 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA:	PATENT NO.				KIN	IND DATE			APPLICATION NO.				NO.		D	ATE		
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		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KP,	KR,	KΖ,	LC,	
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									1	WO 2	003-	US39	606		W 2	0031	212 <	<

OTHER SOURCE(S): MARPAT 141:89100

Title compds. I [wherein V, W, X, Y, and Z = independently N, CR1, with AΒ the proviso that at least one of V and X = N; R = OR7, NR3R4; R1 = independently H, halo, OH, CN, NH2, (halo)alkyl, (halo)alkoxy, alkoxycarbonyl, (di)alkylamino; R3 and R4 = independently H, (un)substituted (aryl)alkyl, alkenyl, alkynyl, alkanoyl, etc.; or R3 or R4 taken together with R5 or R6 forms an (un) substituted heterocycle; or NR3R4 = heterocyclyl; R5 and R6 = independently H, (un)substituted alkyl; or CR5R6 = CO; R7 = H, (aryl)alkyl, alkenyl, alkynyl, alkanoyl, etc.; or R7 taken together with R5 or R6 forms an (un)substituted heterocycle; n =1-3; Ar1 and Ar2 = independently (un)substituted aryl, heterocyclyl; and pharmaceutically acceptable forms thereof] were prepared as modulators of capsaicin receptors, especially the vanilloid receptor 1 (VR1). For example, a solution of [2-(chloromethyl)-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4yl](4-trifluoromethylphenyl)amine⊕HCl and pyrrolidine was heated to 100° for 1 h to give II. In competition binding assays, invention compds. exhibited Ki \leq 1 μM for VR1 expressed in human embryonic kidney (HEK293) cells. Thus, I and their pharmaceutical compns. are useful for treating disorders associated with pathol. receptor activation, such as pain, in humans, domesticated companion animals, and livestock animals (no data).

IT 573686-39-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(VR1 inhibitor; preparation of (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

RN 573686-39-2 CAPLUS

CN 4-Quinazolinamine, 2-(4-pyridinyl)-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (CA INDEX NAME)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:531361 CAPLUS

DOCUMENT NUMBER: 141:76702

TITLE: Combination therapy comprising a heteroarylamine VR1

antagonist and a narcotic analgesic for the treatment

of pain with reduced addictive side effects

INVENTOR(S): Herzberg, Uri; Cortright, Daniel; Hurtt, Mark M.;

Krause, James E.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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									•	WO 2	003-	US37	209	Ţ	W 2	0031	119 -	<
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AΒ The invention relates to compns. comprising a nontoxic vanilloid receptor 1 (VR1) antagonist, optionally in combination with an addictive therapeutic agent, for the treatment of pain. Compns. and methods are further provided for inhibiting the development of tolerance to addictive therapeutic agents (especially narcotic analgesics) in patients treated with such agents, for minimizing adverse effects (e.g., dependence) resulting from treatment with such addictive agents, and for enhancing pain relief resulting from narcotic analgesic administration. Patients may be treated with a VR1 antagonist before, during, or after administration of the addictive therapeutic agent to prevent, decrease the severity of, delay, or treat tolerance and/or other adverse effects of the addictive agent in the patient. Examples include synthetic methods and limited data for the preparation of representation heteroarylamine VR1 antagonists, as well as capsaicin receptor binding assays and numerous pain model assays. For instance, coupling of 7-bromo-4-chloroquinazoline with 2-amino-5-trifluoromethylpyridine, followed by addition of 3-fluoro-2-tributylstannylpyridine provided I. In a bioassay testing the inhibition of tolerance to morphine, rats receiving morphine plus II exhibited statistically significantly higher withdrawal thresholds than any other treatment group, indicating that the VR1 antagonist prevents tolerance to repeated morphine dosing.

Ι

IT 573686-39-2

RL: PRPH (Prophetic)

(Combination therapy comprising a heteroarylamine VR1 antagonist and a narcotic analgesic for the treatment of pain with reduced addictive side effects)

RN 573686-39-2 CAPLUS

CN 4-Quinazolinamine, 2-(4-pyridinyl)-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (CA INDEX NAME)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:931342 CAPLUS

DOCUMENT NUMBER: 140:791

TITLE: Treatment of fibroproliferative disorders using

TGF- β inhibitors

INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Higgins, Linda

S.; Kapoun, Ann M.; Liu, David Y.; Schreiner, George

F.; Protter, Andrew A.; Tran, Thomas-Toan

PATENT ASSIGNEE(S): Scios, Inc., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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										,	WO 2	003-	US15	514	1	W 2	0030	516 <-	
סשעדר	90	TIDOF	(9).			MAD.	DAT	1/10 •	791										

OTHER SOURCE(S): MARPAT 140:791

AB The invention concerns methods of treating fibroproliferative disorders associated with TGF- β signaling, by administering non-peptide small molinhibitors of TGF- β specifically binding to the type I TGF- β receptor (TGF β -R1). Preferably, the inhibitors are quinazoline

derivs. The invention also concerns methods for reversing the effect of TGF- β mediated cell activation on the expression of a gene associated with fibrosis, comprising contacting a cell or tissue in which the expression of such gene is altered as a result of TGF- β mediated cell activation, with a non-peptide small mol. inhibitor of TGF- β , specifically binding a TGF β -R1 receptor kinase present in the cell or tissue.

IT 157862-99-2 627535-99-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(treatment of fibroproliferative disorders using $TGF-\beta$ inhibitors)

RN 157862-99-2 CAPLUS

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 627535-99-3 CAPLUS

CN 4-Quinazolinamine, N-2-naphthalenyl-2-(4-pyridinyl)- (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:591156 CAPLUS

DOCUMENT NUMBER: 139:149640

TITLE: Preparation of substituted quinazolin-4-ylamine

analogs as VR1 capsaicin receptor antagonists for

relieving pain

INVENTOR(S): Bakthavatchatam, Rajagopal; Blum, Charles A.;

Brielmann, Harry L.; Caldwell, Timothy M.; De

Lombaert, Stephane

PATENT ASSIGNEE(S): Neurogen Corporation, USA SOURCE: PCT Int. Appl., 294 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2003062209
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PRIORITY APPLN. INFO.:
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A3 20060201
                                            US 2003-347210
                                            US 2006-345926
OTHER SOURCE(S):
                       MARPAT 139:149640
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GΙ

AΒ Substituted quinazolin-4-ylamine analogs (shown as I; variables defined below; e.g. (4-trifluoromethylphenyl)[7-(2trifluoromethylphenyl)quinazolin-4-yl]amine) are provided. Such compds. are ligands that may be used to modulate VR1 capsaicin receptor activity in vivo or in vitro (no data), and are particularly useful in the treatment of conditions associated with pathol. receptor activation in humans, domesticated companion animals and livestock animals. Pharmaceutical compns. and methods for using them to treat such disorders are provided, as are methods for using such ligands for receptor localization studies. For I; V, X, W, Y and Z are each independently N or CR1, with the proviso that at least one of V and X is N; U is N or CR2, with the proviso that if V and X are N, then U is CR2; R1 = H, halogen, hydroxy, amino, C1-C8 alkyl, haloC1-C8alkyl, C1-C8alkoxy, haloC1-C8alkoxy and mono- and di(C1-C8alkyl)amino. R2 = (i) H, halogen, cyano, or -COOH; (ii) C1-C8alkanoyl, C2-C8alkanone, or C1-C8carbamate, each of which is

(un) substituted with 1-9 substituents = Rb, or (iii) -Rc-M-A-Ry, wherein: Rc is C0-C3alkyl; M is a bond, N(Rz), O, S, S02, (C:0)pN(Rz), N(Rz)(C:0)p, SO2N(Rz), or N(Rz)SO2, wherein p is 0 or 1; A is a bond or C1-C8alkyl, (un) substituted with 1-3 Rb. Ry and Rz, if present, are: (a) independently H, C1-C8alkyl, C2-C8alkenyl, C2-C8alkynyl, C6-C10arylC1-C8alkyl, C2-C8alkyl ether, C1-C8alkoxy, a 4- to 10-membered carbocycle or heterocycle, or joined to R1 to form a 4- to 10-membered carbocycle or heterocycle, wherein each Ry and Rz = (un)substituted with 1-9 Rb; or (b) joined to form a 4- to 10-membered carbocycle or heterocycle that is (un)substituted with 1-9 Rb; Ar2 is a 5- to 7-membered aromatic heterocycle, (un) substituted with 1-3 LRa. Ar1 is a 5- to 10-membered aromatic carbocycle or heterocycle, (un) substituted with 1-3 LRa; L = bond, -O-, -C(O)-, -OC(O)-, -C(O)O-, -O-C(O)O-, -S(O)m-, -NRx-,-C(O)NHRx-, -NHRxC(O)-, -NRxS(O)m-, -S(O)mNRx- and -N[S(O)mRx]S(O)m-; wherein m = 0, 1 and 2; and Rx = H and C1-C8alkyl; Ra = (i) H, halogen, cyano and nitro; and (ii) C1-C8alkyl, C2-C8alkenyl, C2-C8alkynyl, C2-C8alkyl ether, 3- to 10-membered heterocycles, mono- and di(C1-C8alkyl)amino and (3- to 10-membered heterocycle)C1-C6 alkyl, each of which is (un)substituted with 1-9 Rb. Rb = hydroxy, halogen, amino, aminocarbonyl, amido, cyano, nitro, C1-C8alkyl, C1-C8alkoxy, C1-C8alkylthio, C1-C8alkyl ether, hydroxyC1-C8alkyl, haloC1-C8alkyl, Ph, phenyl(C1-C8alkyl), mono and di(C1-C6 alkyl)amino, (SO2)C1-C8alkyl, 5- to 7-membered heterocycle and (5- to 7-membered heterocycle)(C1-C8alkyl). Although the methods of preparation are not claimed, many example prepns. and characterization data for >500 examples of I are included. 573686-39-2P, [2-Pyridin-4-yl-7-(3-trifluoromethylpyridin-2-

573686-39-2P, [2-Pyridin-4-yl-7-(3-trifluoromethylpyridin-2yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PAC
(Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic
use); ANST (Analytical study); BIOL (Biological study); PREP
(Preparation); USES (Uses)

(drug candidate and receptor detector; preparation of substituted quinazolin-4-ylamine analogs as VR1 capsaicin receptor antagonists for relieving pain and for detecting receptors)

RN 573686-39-2 CAPLUS

CN

4-Quinazolinamine, 2-(4-pyridinyl)-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (CA INDEX NAME)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:845560 CAPLUS

DOCUMENT NUMBER: 137:353051

TITLE: Preparation of quinazolines as TGF- β and/or

p38- α kinase inhibitors

INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Perumattam,

John J.; Schreiner, George F.; Liu, David Y.; Lewicki,

John A.

PATENT ASSIGNEE(S): Scios, Inc., USA

SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 6,184,226.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA.	TENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US	6476031	B1	20021105	US 1999-383825	1999082	- 7 <
US	6184226	В1	20010206	US 1998-141916	1998082	8
CN	1152867	С	20040609	CN 1999-811659	1999082	7 <
AT	342256	T	20061115	AT 1999-949568	1999082	7 <
ES	2274642	Т3	20070516	ES 1999-949568	1999082	7 <
US	6277989	B1	20010821	US 2000-525034	2000031	4 <
US	20030069248	A1	20030410	US 2001-969936	2001100	2 <
US	20020161010	A1	20021031	US 2001-972582	2001100	5 <
US	6903096	В2	20050607			
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US	7345045	В2	20080318			
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PRIORIT	Y APPLN. INFO.:			US 1998-141916	A2 1998082	8 <
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OTHER SOURCE(S): MARPAT 137:353051

GΙ

$$\begin{bmatrix} L \downarrow_n Ar \\ Z \downarrow_n \\ A \downarrow_n \\ Z \downarrow_n \\ R^3 \quad I \end{bmatrix}$$

AB Title compds. I [R3 = (un)substituted aromatic; Ar = (un)substituted monocyclic or polycyclic aromatic; L = S(CR22)m, NR1SO2(CR22)1, SO2(CR22)m, etc.; Z = CR2, N with the provisos that no more than two Z positions in ring A are N and wherein two adjacent Z positions in ring A cannot be N; R2 = H, alkyl, alkenyl, etc.; l = 0-3; m = 0-4; n = 1] and their pharmaceutically acceptable salts were prepared For example, condensation of chloroquinazoline II and 4-aminopyridine afforded claimed quinazoline III. In p38- α kinase inhibition studies, 9-examples of compds. I

exhibited IC50 values in the range of 0.1-1.5 $\mu M.$ Also, the specificity of compds. I for p38- α was assessed by their ability to inhibit other kinases, e.g., p38-y JNK1, PKA, PKC, PK(PKD), cck2 and EGF-R, with IC50 values ranging from 4.2 - >500 $\mu M.$ Compds. I are useful anti-inflammatory agents and in the treatment of fibroproliferative diseases.

IT 157862-99-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinazolines as TGF- $\!\beta$ and/or p38- $\!\alpha$ kinase inhibitors)

RN 157862-99-2 CAPLUS

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:754381 CAPLUS

DOCUMENT NUMBER: 137:279208

TITLE: Preparation of (indazol-5-ylamino)quinazolines as

Rho-kinase inhibitors

INVENTOR(S): Nagarathnam, Dhanapalan; Asgari, Davoud; Shao,

Jianxing; Liu, Xiao-Gao; Khire, Uday; Wang, Chunguang; Hart, Barry; Boyer, Stephen; Weber, Olaf; Lynch, Mark;

Bankston, Donald

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA:	TENT :	NO.			KIN	D	DATE		APPLICATION NO.						DATE 			
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PRIORITY APPLN. INFO.:
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                                                              B1 20020322 <--
                                                              B1 20020322 <--
                                            US 2002-103566
                                            WO 2002-US8659
                                                              W 20020322 <--
                                            US 2002-252369
                                                              A 20020924 <--
                                            EP 2003-752497
                                                              A3 20030924 <--
                                            WO 2003-752497 AS 20030924 <--
OTHER SOURCE(S): CASREACT 137:279208; MARPAT 137:279208
GΙ
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Title compds. I [Y = N, CR17; X = alkyl, alkoxy, thioalkoxy, amido, etc.; p = 0-3; a, c = CR5, NR6, etc.; b = CR5, N; A = H, halo, carboxy, cyano, alkoxy, etc.; B = (un)substituted up to 3 times in any position by R5; R1,6 = H, alkyl; R2-5 = H, alkyl, alkenyl; R17 = H, alkyl, CN with provisions] were prepared For instance, 2,4-Dichloroquinazoline (preparation given) was reacted with 5-aminoindazole (THF/H2O, KOAc) to give 2-(N-(1H-indazol-5-yl)amino)-4-chloroquinazoline in 92% yield. This was coupled to 2,4-dichlorophenylboronic acid (ethylene glycol di-Me ether, Pd(dppf)Cl2, NaHCO3, reflux) to give II. I are rho-kinase inhibitors and are useful for inhibiting tumor growth, treating erectile dysfunction and coronary heart disease.

IT 461037-54-7P, 5-Fluoro-N-(1H-indazol-5-yl)-2-(4-pyridinyl)-4-quinazolinamine 461037-55-8P 461037-82-1P,
N-(1H-Indazol-5-yl)-7-methyl-2-(4-pyridinyl)-4-quinazolinamine 461037-83-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(rho-kinase inhibitor; preparation of (indazol-5-ylamino)quinazolines as Rho-kinase inhibitors)

RN 461037-54-7 CAPLUS

CN 4-Quinazolinamine, 5-fluoro-N-1H-indazol-5-yl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 461037-55-8 CAPLUS

CN 4-Quinazolinamine, 5-fluoro-N-1H-indazol-5-yl-2-(4-pyridinyl)-, 2,2,2-trifluoroacetate (1:3) (CA INDEX NAME)

CM 1

CRN 461037-54-7 CMF C20 H13 F N6

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 461037-82-1 CAPLUS

CN 4-Quinazolinamine, N-1H-indazol-5-yl-7-methyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 461037-83-2 CAPLUS

CN 4-Quinazolinamine, N-1H-indazol-5-yl-7-methyl-2-(4-pyridinyl)-, 2,2,2-trifluoroacetate (1:3) (CA INDEX NAME)

CM 1

CRN 461037-82-1 CMF C21 H16 N6

CM 2

CRN 76-05-1 CMF C2 H F3 O2

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:158388 CAPLUS

DOCUMENT NUMBER: 136:200203

TITLE: Preparation of 4-aminoquinazolines for use in

inhibiting neoplastic cells and related conditions

INVENTOR(S): Pamukcu, Rifat; Piazza, Gary

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont. of U.S. Ser. No.

60,444, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020025968 PRIORITY APPLN. INFO.:	A1	20020228	US 2001-952769 US 1998-60444 B:	20010914 < 1 19980415 <
OTHER SOURCE(S): GI	MARPAT	136:200203		

$$(R^4)_n$$
 N
 A
 $Z-CyB-(R^3)_m$
 I

HC
$$\equiv$$
 C N N N II

AB Title compds. I [wherein R1 = H or alkyl; Y = alkylene; A = ORa or S(O)pRa; Ra = alkylhydroxy; p = 0-2; Z = single bond, methylene, ethylene, vinylene, or ethynylene; CyB = heterocyclic ring; R3 = H, alkyl, alkoxy, halo, or CF3; R4 = H, alkyl, alkoxy, CO2H, carboxy ester, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, ethynyl, hydroxymethyl, acetyl, or (un)substituted sulfamoyl, carbamoyl, etc.; m and n = independently 1-2; or pharmaceutically acceptable salts or hydrates thereof] were prepared for inhibiting neoplastic cells and related conditions. For example, amination of 2,4-dichloro-6-(2-triethylsilylethynyl)quinazolin-2,4-dione (preparation given) with 2-methoxyethylamine in CHC13, followed by addition of imidazole in EtOH and deprotection using NBu4F, afforded II. I are useful in the treatment of precancerous and cancerous lesions, including malignant melanomas, breast cancer, and colon cancer (no data).

IT 157862-99-2 157863-22-4 1102370-13-7

RL: PRPH (Prophetic)

(Preparation of 4-aminoquinazolines for use in inhibiting neoplastic cells and related conditions)

RN 157862-99-2 CAPLUS

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 157863-22-4 CAPLUS

CN Benzoic acid, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 1102370-13-7 CAPLUS

CN 4-Quinazolinamine, N-methyl-N-phenyl-2-(4-pyridinyl)-, hydrochloride (1:2) (CA INDEX NAME)

●2 HC1

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:161275 CAPLUS

DOCUMENT NUMBER: 132:194387

TITLE: Preparation of quinazolines as $p38-\alpha$ kinase and

TGF- β inhibitors

INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Perumattam,

John J.; Schreiner, George F.; Liu, David Y.; Lewicki,

John A.

PATENT ASSIGNEE(S): Scios Inc., USA

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA:	PATENT NO.			KINI)	DATE A			APPLICATION NO.					DATE			
	20000124 20000124								 WO 1	999-	US19	846		1	9990	827	<
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	1035897					2007	0601			2001-					0010	904	<
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										999-					9990		
HER S	OURCE(S):			MARI	PAT	132:	1943	87									

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AB Title compds. [I; R = ZR1; R1 = (un)substituted cyclic (hetero)aliphatic group, -(hetero)aryl; R3 = noninterfering substituent (sic); R4R5 = atoms to complete a 6-membered aromatic ring containing 0, 1, or 2 nonadjacent N atoms

and noninterfering substituent(s) (sic); z = bond or linker (sic); Z3 = CR2 or N; R2 = noninterfering substituent (sic)] were prepared. Thus, prepared, e.g., 4-(4-pyridinylamino)-2-phenylquinazoline was described. Data for biol. activity of I were given.

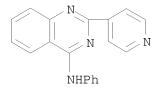
IT 157862-99-2

RL: PRPH (Prophetic)

(Preparation of quinazolines as p38- α kinase and TGF- β inhibitors)

RN 157862-99-2 CAPLUS

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:795361 CAPLUS

DOCUMENT NUMBER: 124:29779

ORIGINAL REFERENCE NO.: 124:5715a,5718a

TITLE: 4-Aminoquinazoline derivatives as inhibitors of cGMP

phosphodiesterase and TXA2 synthetase

INVENTOR(S): Lee, Sung J.; Konishi, Yoshitaka; Macina, Orest T.;

Kondo, Kigen; Yu, Dingwei T.

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: U.S., 42 pp. Cont.-in-part of U.S. Ser. No. 76,431,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5439895	A	19950808	US 1993-154691	19931119 <
JP 06192235	A	19940712	JP 1993-197039	19930714 <
CA 2100626	A1	19940116	CA 1993-2100626	19930715 <
KR 191416	В1	19990615	KR 1993-13549	19930715 <
AT 208771	T	20011115	AT 1993-305557	19930715 <
ES 2167325	Т3	20020516	ES 1993-305557	19930715 <
JP 08099962	A	19960416	JP 1995-264667	19950920 <
JP 2923742	В2	19990726		
PRIORITY APPLN. INFO.:			US 1992-913473	B2 19920715 <
			US 1993-76431	B2 19930614 <

OTHER SOURCE(S): MARPAT 124:29779

GΙ

$$(R^4)_n$$
 N
 $Y-A$
 N
 $Z-CyB-(R^3)_m$
 I

AB The compds. of the formula I and acid addition salts thereof, salts thereof, and hydrates thereof wherein R1 is hydrogen or C1-4 alkyl; Y is C1-6 alkylene; A is ORO or S(O)pRO, in which RO is C1-4 alkyl-hydroxy; p is 0-2; Z is single bond, methylene, ethylene, vinylene or ethynylene; CyB is (1) 7-membered, unsatd. or partially saturated, monocyclic hetero ring containing

TT

as hetero atoms, one, two or three nitrogen atoms, (2) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms, two or

three nitrogen atoms, (3) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atom, one nitrogen atom, (4) 4- or 5-membered, unsatd. or partially saturated, monocyclic hetero ring containing

hetero atoms, one, two or three nitrogen atoms, or (5) 4-7 membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

one or two oxygen atoms, or one or two sulfur atoms; R3 = e.g., H, C1-4 alkyl, C1-4 alkoxy; R4 = e.g., H, C1-4 alkyl, C1-4 alkoxy; and m and n independently are 1 or 2; with the proviso that (1) a CyB ring does not bond to Z through a nitrogen atom in the CyB ring when Z is vinylene or ethynylene, have inhibitory effect on cGMP-PDE, and addnl. on TXA2 synthetase. Thus, e.g., 2-(1-imidazolyl)-4-[2-(2-hydroxyethoxy)ethyl]amino-6-ethynylquinazoline.2HCl (II.2HCl) (prepared by desilylation of a silylacetylene precursor) exhibited inhibitory effect on

cGMP-PDE and TXA2 synthetase with IC50 = 4.6 + 10-8 M and 1.33 + 10-6 M, resp. Pharmaceutical formulations were given.

157862-99-2P 157863-22-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(4-aminoquinazoline derivs. as inhibitors of cGMP phosphodiesterase and TXA2 synthetase)

RN 157862-99-2 CAPLUS

as

ΙT

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 157863-22-4 CAPLUS

CN Benzoic acid, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:761961 CAPLUS

DOCUMENT NUMBER: 123:340173

ORIGINAL REFERENCE NO.: 123:61059a,61062a

TITLE: 4-Aminoquinazoline derivatives as inhibitors of cyclic

guanosine 3',5'-monophosphate phosphodiesterase and

thromboxane A2 synthetase

INVENTOR(S):
Lee, Sung J.; Konishi, Yoshitaka; Macina, Orest T.;

Kondo, Kigen; Yu, Dingwei T.

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: U.S., 44 pp. Cont.-in-part of U.S. Ser. No. 76,431,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 5436233	A	19950725	US 1993-154518	19931119 <
	JP 06192235	A	19940712	JP 1993-197039	19930714 <
	CA 2100626	A1	19940116	CA 1993-2100626	19930715 <
	KR 191416	B1	19990615	KR 1993-13549	19930715 <
	AT 208771	T	20011115	AT 1993-305557	19930715 <
	ES 2167325	Т3	20020516	ES 1993-305557	19930715 <
	JP 08099962	A	19960416	JP 1995-264667	19950920 <
	JP 2923742	В2	19990726		
PRIO:	RITY APPLN. INFO.:			US 1992-913473 B2	2 19920715 <
				US 1993-76431 B2	2 19930614 <
_					

OTHER SOURCE(S): CASREACT 123:340173; MARPAT 123:340173

GΙ

$$(R^4)_n$$
 N
 $Y-A$
 N
 $Z-CvB-(R^3)_m$
 I

AB Title compds. I [R1 is H, C1-4 alkyl; Y is a single bond or C1-6 alkylene; A is (i) CyA-(R2)l, (ii) ORO or S(O)pR0 in which R0 is R0A or R0B; R0A is CyA-(R2)l; R0B is H or C1-4 alkyl; p is 0-2; CyA is, e.g., (1) 3-7 membered, saturated or unsatd., monocyclic carbocyclic ring, (2) 7-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

one nitrogen atom, one nitrogen and one oxygen atoms, two nitrogen and one oxygen atoms, or one nitrogen and two oxygen atoms, (3) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

one nitrogen and one oxygen atoms, two nitrogen and one oxygen atoms, or one nitrogen and two oxygen atoms; R2 is R2A or R2B; R2A is, e.g., CF3, OCF3; R2B is, e.g., H, C1-4 alkyl, C1-4 alkoxy; Z is ZA or ZB, ZA is methylene, ethylene, ethynylene; ZB is a single bond; CyB is, e.g., (1) 7-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms, one, two or three nitrogen atoms, (2) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

two or three nitrogen atoms, (3) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as a hetero atom, one nitrogen atom; R3 = e.g., H, C1-4 alkyl; R4 = e.g., NHSO2R11, R11 = e.g., C1-4 alkyl; l, m, n are independently 1 or 2 (with provisos)] are provided as inhibitors of cGMP-PDE and TXA2 synthetase. Thus, e.g., treatment of $2-(1-i\text{midazolyl})-4-(2-\text{methoxyethyl}) \text{ amino-}6-(2-\text{triethylsilylethynyl}) \text{ quinazoline (preparation given) with tetrabutylammonium fluoride afforded 6-ethynyl-4-(2-methoxyethyl) amino-2-(1-imidazolyl) quinazoline (II); II.2HCl demonstrated inhibition of cGMP-PDE with and TXA2 synthetase with IC50 = <math>4.6+10-8$ and 2.4+10-6 M, resp. Pharmaceutical formulations were given.

IT 157862-99-2P 157863-22-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(4-aminoquinazoline derivs. as inhibitors of cyclic guanosine

3',5'-monophosphate phosphodiesterase and thromboxane A2 synthetase)

RN 157862-99-2 CAPLUS

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 157863-22-4 CAPLUS

CN Benzoic acid, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:605373 CAPLUS

DOCUMENT NUMBER: 121:205373

ORIGINAL REFERENCE NO.: 121:37397a,37400a

TITLE: 4-aminoquinazoline derivatives, and their use as

medicine

INVENTOR(S): Lee, Sung Jai; Konishi, Yoshitaka; Macina, Orest

Taras; Kondo, Kigen; Yu, Dingwei Tim

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 86 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 579496	A1	19940119	EP 1993-305557	19930715 <
EP 579496	B1	20011114		
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IE, IT, LI, LU,	, MC, NL, PT, SE
JP 06192235	A	19940712	JP 1993-197039	19930714 <
CA 2100626	A1	19940116	CA 1993-2100626	19930715 <
KR 191416	B1	19990615	KR 1993-13549	19930715 <
AT 208771	T	20011115	AT 1993-305557	19930715 <
ES 2167325	Т3	20020516	ES 1993-305557	19930715 <
JP 08099962	A	19960416	JP 1995-264667	19950920 <
JP 2923742	В2	19990726		
PRIORITY APPLN. INFO.:			US 1992-913473	A 19920715 <
			US 1993-76431	A 19930614 <

OTHER SOURCE(S): MARPAT 121:205373

GΙ

AB The title compds. I wherein R1 is H or alkyl; Y is bond or alkylene; A is (i) -CyAR2, (ii) -OR0 or -S(O)pR0, R0 = H, alkyl, etc., p is 0-2, (iii) -NR16R17, R16, R17 are H, alkyl; CyA is (1) a 3-7 membered monocyclic carbocyclic ring, (2) a 4-7 membered monocyclic hetero ring containing as hetero atoms, one N atom, one N and one O atoms, two N and one O atoms, or one N and two O atoms, (3) a 4-7 membered monocyclic hetero ring containing as hetero atoms, 1 or 2 O or S atoms, R2 is (1) H, (2) alkyl, (3) alkoxy, (4) -COOR5, in which R5 is H or alkyl, (5) -NR6R7, R6, R7 are H, alkyl, (6) -SO2NR6R7, (7) halogen, (8) CF3, (9) NO2 or (10) CF3O; Z is bond, methylene, ethylene, vinylene or ethynylene; CyB is a heterocyclic ring; R3 is H, alkyl, alkoxy, halogen or CF3; R4 is H, alkyl, alkoxy, etc., and acid addition salts thereof, salts thereof, and hydrates thereof were prepared and have inhibitory effect on cGMP-PDE, or addnl. on TXA2 synthetase. Thus, a representative prepared compound II had inhibitory activity IC50 of $3.6 \times 10-7$ on cGMP-PDE.

IT 157862-99-2P 157863-22-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as cardiovascular agents)

RN 157862-99-2 CAPLUS

CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 157863-22-4 CAPLUS

CN Benzoic acid, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

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SINCE FILE
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CA SUBSCRIBER PRICE

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http://www.cas.org/support/stngen/stndoc/properties.html

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chain nodes :
19
ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17
ring/chain nodes :
18
chain bonds :
7-18 9-12 18-19
ring bonds :
1 - 2 \quad 1 - 6 \quad 2 - 3 \quad 3 - 4 \quad 4 - 5 \quad 5 - 6 \quad 5 - 7 \quad 6 - 10 \quad 7 - 8 \quad 8 - 9 \quad 9 - 10 \quad 12 - 13 \quad 12 - 17 \quad 13 - 14 \quad 14 - 15
15-16 16-17
exact/norm bonds :
7-18 18-19
exact bonds :
9 - 12
normalized bonds :
1-2 \quad 1-6 \quad 2-3 \quad 3-4 \quad 4-5 \quad 5-6 \quad 5-7 \quad 6-10 \quad 7-8 \quad 8-9 \quad 9-10 \quad 12-13 \quad 12-17 \quad 13-14 \quad 14-15
15-16 16-17
isolated ring systems :
containing 1 : 12 :
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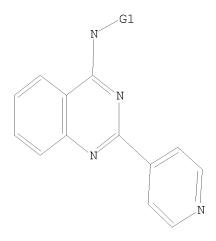
G1:Hy,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom

L7 STRUCTURE UPLOADED

=> d 17 L7 HAS NO ANSWERS L7 STR



G1 Hy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s 17

SAMPLE SEARCH INITIATED 18:10:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 60 TO ITERATE

100.0% PROCESSED 60 ITERATIONS 5 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

PROJECTED ITERATIONS: 736 TO 1664

PROJECTED ANSWERS: 5 TO 234

L8 5 SEA SSS SAM L7

=> s 17 sss full

FULL SEARCH INITIATED 18:10:36 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1114 TO ITERATE

100.0% PROCESSED 1114 ITERATIONS 141 ANSWERS

SEARCH TIME: 00.00.01

L9 141 SEA SSS FUL L7

=> d scan

L9 141 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 4-Quinazolinamine, N-[2-(2,6-dimethyl-4-morpholinyl)-2-methylpropyl]-2-(4-pyridinyl)-

MF C23 H29 N5 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

L9 141 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 4-Quinazolinamine, N,2-di-4-pyridinyl-

MF C18 H13 N5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 141 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 4-Quinazolinamine, N-[(2-methoxy-4-pyridinyl)methyl]-2-(4-pyridinyl)-

MF C20 H17 N5 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 141 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN Ethanol, 2-[(phenylmethyl)[2-(4-pyridinyl)-4-quinazolinyl]amino]-

MF C22 H20 N4 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 141 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN INDEX NAME NOT YET ASSIGNED

MF C21 H20 N8

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 141 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN Acetamide, 2-[ethyl[2-(4-pyridinyl)-4-quinazolinyl]amino]-N-(4-methoxyphenyl)-

MF C24 H23 N5 O2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil cap		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	186.36	462.63
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-9.84

FILE 'CAPLUS' ENTERED AT 18:11:02 ON 24 APR 2009
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FILE COVERS 1907 - 24 Apr 2009 VOL 150 ISS 18 FILE LAST UPDATED: 23 Apr 2009 (20090423/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

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(FILE 'HOME' ENTERED AT 17:35:01 ON 24 APR 2009)

FILE 'REGISTRY' ENTERED AT 17:35:21 ON 24 APR 2009

L1 STRUCTURE UPLOADED

L2 3 S L1

L3 59 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 17:38:43 ON 24 APR 2009

L4 15 S L3

L5 12 S L4 AND (PRY<2004)

L6 0 S 1-12 IBIB ABS HITSTR

FILE 'STNGUIDE' ENTERED AT 17:42:47 ON 24 APR 2009

FILE 'REGISTRY' ENTERED AT 18:09:40 ON 24 APR 2009

L7 STRUCTURE UPLOADED

L8 5 S L7

L9 141 S L7 SSS FULL

FILE 'CAPLUS' ENTERED AT 18:11:02 ON 24 APR 2009

=> s 19 and (pry<2004)

25 L9

4270617 PRY<2004

L10 21 L9 AND (PRY<2004)

=> d 1-21 ibib abs hitstr

L10 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:902403 CAPLUS

DOCUMENT NUMBER: 141:374752

TITLE: Heterocyclic compound modulators of kinases,

particularly Tie-2 kinase, and use in the treatment of

kinase-dependent diseases

INVENTOR(S): Ibrahim, Mohamed; Leahy, James; Sangalang, Joan C.;

Schnepp, Kevin; Shi, Xian; Nuss, John

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIN	D	DATE .			APPLICATION NO.						DATE		
						_									_			
WO	2004	0921	96		A2		2004	1028		WO 2	004-	US10	858		2	0040	408 <-	-
WO 2004092196					А3		2005	0317										
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		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑM,	AZ,	

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2004-230928 AU 2004230928 20041028 20040408 <--Α1 CA 2004-2520323 CA 2520323 Α1 20041028 20040408 <--EP 1610774 A2 20060104 EP 2004-749893 20040408 <--R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR JP 2006523238 Τ 20061012 JP 2006-509820 20040408 <--US 20070161651 20070712 US 2005-552426 20051007 <--Α1 PRIORITY APPLN. INFO.: 20030409 <--US 2003-461446P WO 2004-US10858 A 20040408 OTHER SOURCE(S): MARPAT 141:374752 The invention provides compds. for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. Compds. of the invention inhibit, regulate and/or modulate kinases, particularly Tie-2. Methods of using the compds. and pharmaceutical compns. thereof to treat kinase-dependent diseases and conditions are also an aspect of the invention. Preparation of quinazoline compds. of the invention is described. 18590-70-0P 781615-22-3P 781615-23-4P ΙT 781615-24-5P 781615-25-6P 781615-26-7P 781615-36-9P 781615-37-0P 781615-38-1P 781615-48-3P 781615-55-2P 781615-57-4P 781615-76-7P 781615-77-8P 781615-78-9P 781615-82-5P 781615-83-6P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (heterocyclic compound modulators of kinases, particularly Tie-2 kinase, and use in treatment of kinase-dependent diseases) 18590-70-0 CAPLUS RN 4-Quinazolinamine, N-[2-(4-morpholinyl)ethyl]-2-(4-pyridinyl)- (CA INDEX CN NAME)

RN 781615-22-3 CAPLUS CN 4-Quinazolinamine, N-(cyclohexylmethyl)-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-23-4 CAPLUS

CN Ethanol, 2-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 781615-24-5 CAPLUS

CN 1-Propanol, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 781615-25-6 CAPLUS

CN 4-Quinazolinamine, N-[(4-fluorophenyl)methyl]-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-26-7 CAPLUS

CN 1,2-Ethanediamine, N1,N1-dimethyl-N2-[2-(4-pyridinyl)-4-quinazolinyl]- (CA INDEX NAME)

RN 781615-36-9 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[2-(4-pyridiny1)-4-quinazoliny1]amino]-, 1,1-dimethylethyl ester (CA INDEX NAME)

RN 781615-37-0 CAPLUS

CN 4-Quinazolinamine, 2-(4-pyridinyl)-N-[(2,4,6-trimethoxyphenyl)methyl](CA INDEX NAME)

RN 781615-38-1 CAPLUS CN 4-Quinazolinamine, N-4-piperidinyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-48-3 CAPLUS CN 4-Quinazolinamine, N-[2-(1-piperazinyl)ethyl]-2-(4-pyridinyl)- (CA INDEX NAME)

RN 781615-55-2 CAPLUS
CN 1,2-Propanediol, 3-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-57-4 CAPLUS

CN 1-Propanol, 2-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-76-7 CAPLUS

CN Benzenepropanol, β -[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, (β R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-77-8 CAPLUS

CN Benzenepropanol, β -[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, (β S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-78-9 CAPLUS

CN Ethanol, 2-[(phenylmethyl)[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 781615-82-5 CAPLUS

CN 1-Piperazineethanol, 4-[[2-(4-pyridinyl)-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 781615-83-6 CAPLUS

CN 4-Quinazolinamine, N-1-piperidinyl-2-(4-pyridinyl)- (CA INDEX NAME)

TT 781615-20-1 781615-58-5 781615-66-5 781615-69-8 781615-70-1 781615-71-2

781615-72-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(heterocyclic compound modulators of kinases, particularly Tie-2 kinase, and use in treatment of kinase-dependent diseases)

RN 781615-20-1 CAPLUS

CN 4-Quinazolinamine, 2-(4-pyridinyl)-N-[2-(1-pyrrolidinyl)ethyl]- (CA INDEX NAME)

RN 781615-58-5 CAPLUS

CN 2-Propanol, 1-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-66-5 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-(3S)-3-piperidinyl-2-(4-pyridinyl)(CA INDEX NAME)

Absolute stereochemistry.

RN 781615-69-8 CAPLUS

CN 1-Butanol, 2-[[2-(3-methoxy-4-pyridinyl)-7-methyl-4-quinazolinyl]amino]-3-methyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-70-1 CAPLUS

CN 1-Butanol, 2-[[2-(3-methoxy-4-pyridinyl)-7-methyl-4-quinazolinyl]amino]-3-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-71-2 CAPLUS

CN Benzeneethanol, β -[[2-(3-methoxy-4-pyridinyl)-7-methyl-4-quinazolinyl]amino]-, (β S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 781615-72-3 CAPLUS

CN Benzeneethanol, β -[[2-(3-methoxy-4-pyridinyl)-7-methyl-4-quinazolinyl]amino]-, (β R)- (CA INDEX NAME)

Absolute stereochemistry.

IT 781615-85-8P 781616-05-5P

RL: SPN (Synthetic preparation); PREP (Preparation) (heterocyclic compound modulators of kinases, particularly Tie-2 kinase,

and use in treatment of kinase-dependent diseases)

RN 781615-85-8 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[2-(4-pyridinyl)-4-quinazolinyl]amino]-, 1,1-dimethylethyl ester (CA INDEX NAME)

RN 781616-05-5 CAPLUS

CN 4-Quinazolinamine, N-(3S)-3-piperidinyl-2-(4-pyridinyl)- (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:931342 CAPLUS

DOCUMENT NUMBER: 140:791

TITLE: Treatment of fibroproliferative disorders using

 $TGF-\beta$ inhibitors

INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Higgins, Linda

S.; Kapoun, Ann M.; Liu, David Y.; Schreiner, George

F.; Protter, Andrew A.; Tran, Thomas-Toan

PATENT ASSIGNEE(S): Scios, Inc., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	PATENT NO.					KIND DATE				APPLICATION NO.								
WO	2003	0976	15		A1												516 <	
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		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	
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		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	G₩,	ML_{\prime}	MR,	ΝE,	SN,	TD,	TG	
AU	2003	2293	05		A1		2003	1202		AU 2	003-	2293	05		2	0030	516 <	
US	2004	0038	856		A1		2004	0226		US 2	003-	4404	28		2	0030	516 <	
EP	1511	738			A1		2005	0309		EP 2	003-	7268	92		2	0030	516 <	
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
PRIORIT	Y APP	LN.	INFO	.:						US 2	002-	3817.	20P		P 2	0020	517 <	
												-	-				516 <	
										WO 2	003-	US15	514		W 2	0030	516 <	

OTHER SOURCE(S): MARPAT 140:791

AB The invention concerns methods of treating fibroproliferative disorders associated with TGF- β signaling, by administering non-peptide small mol. inhibitors of TGF- β specifically binding to the type I TGF- β receptor (TGF β -R1). Preferably, the inhibitors are quinazoline derivs. The invention also concerns methods for reversing the effect of TGF- β mediated cell activation on the expression of a gene associated with fibrosis, comprising contacting a cell or tissue in which the expression of such gene is altered as a result of TGF- β mediated cell activation, with a non-peptide small mol. inhibitor of TGF- β , specifically binding a TGF β -R1 receptor kinase present in the cell or tissue.

IT 474289-44-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of fibroproliferative disorders using $TGF-\beta$ inhibitors)

RN 474289-44-6 CAPLUS

CN 4-Quinazolinamine, N,2-di-4-pyridinyl- (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2003:472388 CAPLUS

DOCUMENT NUMBER: 139:53030

TITLE: Pyrimidine-based and quinazoline-based compounds

useful as GSK-3 inhibitors

INVENTOR(S): Choquette, Deborah; Davies, Robert J.; Wannamaker,

Marion W.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

GΙ

PA.	PATENT NO.					KIND DATE			APPLICATION NO.					DATE				
WO	2003	 0497	 39		A1	_	2003	0619							2	0021	209	<
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							SE,											
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							GN,									•	·	
CA	2469	,						~ ,					,			0021	209	<
	2002																	
	2002																	
	2003									US 2	002-	3149	05		2	0021	209	<
	1474						2004											
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							RO,									,	·	
JP	2005															0021	209	<
	2004																	
	2004																	
PRIORIT												3388						
	-								US39									
OTHER SO	OTHER SOURCE(S):						MARPAT 139:53030										-	

AB The invention provides a compound of formula I or a pharmaceutically acceptable derivative thereof [wherein: R1 = (un)substituted 5- to 6-membered monocyclic or 8- to 10-membered bicyclic (hetero)aryl with 0-4 N/O/S atom(s); Q = (un)substituted C1-4 alkylene chain with 0-2 non-adjacent CH2 optionally replaced by SO2 or CO; R2 = certain (un)substituted Ph, thienyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ra, Rb = -T-R3; or RaRb = atoms to complete fused,

partially saturated or aromatic, 5- to 8-membered ring with 0-3 N/O/S atom(s)

and

optionally substituted by oxo, -T-R3, etc.; T = bond or C1-4 alkylene chain; R3 = H, halo, OH or derivs., NH2 or derivs., CN, SH or derivs., CHO or derivs., CO2H or derivs., etc.; including pharmaceutically acceptable derivs. and prodrugs]. The compds. are inhibitors of protein kinases, particularly GSK-3 (glycogen synthase kinase 3) mammalian protein kinases. The invention also provides pharmaceutically acceptable compns. comprising the compds. of the invention, and methods of utilizing the compds. and compns. in the treatment of various protein kinase-mediated disorders, such as diabetes, cancer, stroke, and Alzheimer's disease. A table of over 200 compds. I is given in claims. Prepns. of 37 compds. are described in detail. For instance,

4-chloro-2-(2-trifluoromethylphenyl)quinazoline was thermally condensed with 6-(2-aminoethylamino)nicotinonitrile (neat, approx. 140°) to give 49% title compound II. In a test for inhibition of GSK-3 β in vitro, 17 compds. I, including II, had Ki < 0.1 μM , and 16 compds. had Ki of 0.1 to 1.0 μM .

IT 544676-80-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of pyrimidine-based compds. useful as GSK-3 inhibitors)

RN 544676-80-4 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[[2-[[2-(4-pyridinyl)-4-quinazolinyl]amino]ethyl]amino]- (CA INDEX NAME)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:849586 CAPLUS

DOCUMENT NUMBER: 137:370099

TITLE: Preparation of 3-aminopyrazolo[3,4-c]pyridazines as

inhibitors of glycogen synthase kinase-3 and crystal

structures of $gsk-3\beta$ protein and protein

complexes

INVENTOR(S): Ter Haar, Ernst; Swenson, Lovorka; Green, Jeremy;

Arnost, Michael J.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 778 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	PATENT NO.						KIND DATE				APPLICATION NO.									
		2002				A2		2002	1107								0020	429	<	
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		W:							AZ,											
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			•	•		•		,	ZA,	•										
		RW:							SD,											
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	CA 2444882																			
		2002															0020	429	<	
Ü	JS	2003									US 2	002-	1352	55		2	0020	429	<	
		7390	808			В2		2008	0624											
F	ΣP	1435	957			A2		2004	0714		EP 2	002-	7290	56		2	0020	429	<	
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,		
									MK,											
J	JΡ	2005	5047	31		T		2005	0217		JP 2	002-	5853	80		2	0020	429	<	
M	ΙX	2003	0099	57		Α		2005	0725		MX 2	003-	9957			2				
Ü	JS	2008	0262	205		A1		2008	1023		US 2	-800	7991	7		2	0800	328	<	
PRIORI	RIORITY APPLN. INFO.:										US 2	001-	2873	66P		P 2	0010	430	<	
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											US 2	002-	3618	99P		P 2	0020	227	<	
										02-135255 A3 20020429 <-				<						
																W 20020429 <				
OMITTED	0.0	NI DOD	(0)			1 (7) (7)	WO 2002-0513311 W 20020429													

OTHER SOURCE(S): MARPAT 137:370099

GΙ

AB Title compds. [I; R1 = H, RCO, RO2C, (substituted) aliphatyl, carbocyclyl, heterocyclyl, heteroaryl, etc.; R2, R3 = H, (substituted) aliphatyl, carbocyclyl, heteroaryl, aryl, aralkyl, heteroaryl, heteroaralkyl, NR2, NRCOR, SR, OR, CF3, halo, NO2, cyano, etc.; R = H, (substituted) aliphatyl, carbocyclyl, heterocyclyl, aryl, aralkyl, heteroaryl, heteroaralkyl], were prepared Thus, 3-chloro-4-cyano-5,6-diphenylpyridazine was refluxed with N2H4 in EtOH to give 3-amino-4,5-diphenyl-1H-pyrazolo[3,4-c]pyridazine. The latter inhibited gsk-3 with Ki \leq 0.1 μ M.

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(crystal structure determination; preparation of pyrazolopyridazines as inhibitors

of gsk-3 and crystal structures of gsk-3 β protein and protein complexes)

474381-74-3 CAPLUS RN

Kinase (phosphorylating), glycogen synthetase (human isoenzyme 3β), CN compd. with N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-4-quinazolinamine(1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 474231-10-2 CMF Unspecified

CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

2 CM

404828-10-0 CRN CMF C17 H14 N6

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:845560 CAPLUS

DOCUMENT NUMBER: 137:353051

TITLE: Preparation of quinazolines as $TGF-\beta$ and/or

 $p38-\alpha$ kinase inhibitors

INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Perumattam,

John J.; Schreiner, George F.; Liu, David Y.; Lewicki,

John A.

PATENT ASSIGNEE(S):

Scios, Inc., USA U.S., 37 pp., Cont.-in-part of U.S. 6,184,226. SOURCE:

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6476031	B1	20021105	US 1999-383825	19990827 <

US (6184226	B1	20010206	US	1998-141916		19980828	
CN 3	1152867	С	20040609	CN	1999-811659		19990827	<
AT 3	342256	T	20061115	ΑT	1999-949568		19990827	<
ES 2	2274642	Т3	20070516	ES	1999-949568		19990827	<
US 6	6277989	B1	20010821	US	2000-525034		20000314	<
US 2	20030069248	A1	20030410	US	2001-969936		20011002	<
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				US	2001-969936	В1	20011002	<
				US	2001-972582	АЗ	20011005	<

OTHER SOURCE(S):

MARPAT 137:353051

GΙ

$$\begin{bmatrix} L \downarrow_n Ar \\ Z \downarrow_n Ar \\ A \downarrow_n B \\ Z \downarrow_n N \downarrow_{R3} I \end{bmatrix}$$

Title compds. I [R3 = (un)substituted aromatic; Ar = (un)substituted monocyclic or polycyclic aromatic; L = S(CR22)m, NR1SO2(CR22)1, SO2(CR22)m, etc.; Z = CR2, N with the provisos that no more than two Z positions in ring A are N and wherein two adjacent Z positions in ring A cannot be N; R2 = H, alkyl, alkenyl, etc.; l = 0-3; m = 0-4; n = 1] and their pharmaceutically acceptable salts were prepared For example, condensation of chloroquinazoline II and 4-aminopyridine afforded claimed quinazoline III. In p38- α kinase inhibition studies, 9-examples of compds. I exhibited IC50 values in the range of 0.1-1.5 μ M. Also, the specificity of compds. I for p38- α was assessed by their ability to inhibit other kinases, e.g., p38-y JNK1, PKA, PKC, PK(PKD), cck2 and EGF-R, with IC50 values ranging from 4.2 - >500 μ M. Compds. I are useful anti-inflammatory agents and in the treatment of fibroproliferative diseases.

IT 474289-44-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinazolines as TGF- β and/or p38- α kinase inhibitors)

RN 474289-44-6 CAPLUS

CN 4-Quinazolinamine, N,2-di-4-pyridinyl- (CA INDEX NAME)

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:754381 CAPLUS

DOCUMENT NUMBER: 137:279208

TITLE: Preparation of (indazol-5-ylamino)quinazolines as

Rho-kinase inhibitors

INVENTOR(S): Nagarathnam, Dhanapalan; Asgari, Davoud; Shao,

Jianxing; Liu, Xiao-Gao; Khire, Uday; Wang, Chunguang; Hart, Barry; Boyer, Stephen; Weber, Olaf; Lynch, Mark;

Bankston, Donald

PATENT ASSIGNEE(S): Bayer Corporation, USA SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

WO 2002076976 A2 20021003 WO 2002-US8659 20020322 < WO 2002076976 A3 20021212 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,	PATENT NO.	KIND DATE	APPLICATION NO.	DATE			
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,			5K, 5L, 10, 1H, 1K, 11,	12, UA, UG,			
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PRIORITY APPLN. INFO.:
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                                                    CASREACT 137:279208; MARPAT 137:279208
OTHER SOURCE(S):
GΙ
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Title compds. I [Y = N, CR17; X = alkyl, alkoxy, thioalkoxy, amido, etc.; p = 0-3; a, c = CR5, NR6, etc.; b = CR5, N; A = H, halo, carboxy, cyano, alkoxy, etc.; B = (un)substituted up to 3 times in any position by R5; R1,6 = H, alkyl; R2-5 = H, alkyl, alkenyl; R17 = H, alkyl, CN with provisions] were prepared For instance, 2,4-Dichloroquinazoline (preparation given) was reacted with 5-aminoindazole (THF/H2O, KOAc) to give 2-(N-(1H-indazol-5-yl)amino)-4-chloroquinazoline in 92% yield. This was coupled to 2,4-dichlorophenylboronic acid (ethylene glycol di-Me ether, Pd(dppf)Cl2, NaHCO3, reflux) to give II. I are rho-kinase inhibitors and are useful for inhibiting tumor growth, treating erectile dysfunction and coronary heart disease.

IT 461037-54-7P, 5-Fluoro-N-(1H-indazol-5-yl)-2-(4-pyridinyl)-4-quinazolinamine 461037-55-8P 461037-82-1P,
N-(1H-Indazol-5-yl)-7-methyl-2-(4-pyridinyl)-4-quinazolinamine 461037-83-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(rho-kinase inhibitor; preparation of (indazol-5-ylamino)quinazolines as Rho-kinase inhibitors)

RN 461037-54-7 CAPLUS

CN 4-Quinazolinamine, 5-fluoro-N-1H-indazol-5-yl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 461037-55-8 CAPLUS

CN 4-Quinazolinamine, 5-fluoro-N-1H-indazol-5-yl-2-(4-pyridinyl)-, 2,2,2-trifluoroacetate (1:3) (CA INDEX NAME)

CM 1

CRN 461037-54-7 CMF C20 H13 F N6

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 461037-82-1 CAPLUS

CN 4-Quinazolinamine, N-1H-indazol-5-yl-7-methyl-2-(4-pyridinyl)- (CA INDEX NAME)

RN 461037-83-2 CAPLUS

CN 4-Quinazolinamine, N-1H-indazol-5-yl-7-methyl-2-(4-pyridinyl)-, 2,2,2-trifluoroacetate (1:3) (CA INDEX NAME)

CM 1

CRN 461037-82-1 CMF C21 H16 N6

CM 2

CRN 76-05-1 CMF C2 H F3 O2

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:615578 CAPLUS

DOCUMENT NUMBER: 137:154942

TITLE: Preparation of novel quinazoline derivatives for

preventing or treating inflammatory diseases caused by

bacterial DNA

INVENTOR(S): Kisanuki, Sumitsugu; Tomizawa, Hideyuki; Isobe,

Yoshiaki

PATENT ASSIGNEE(S): Japan Energy Corp., Japan PCT Int. Appl., 96 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 2002062767 Α1 20020815 WO 2002-JP1045 20020207 <--W: AU, CA, JP, NZ, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR AU 2002230181 Α1 20020819 AU 2002-230181 20020207 <--PRIORITY APPLN. INFO.: JP 2001-30973 A 20010207 <--WO 2002-JP1045 W 20020207 <--

MARPAT 137:154942 OTHER SOURCE(S):

GΙ

Disclosed are medicinal compns. for preventing or treating inflammatory AΒ diseases caused by bacterial DNA which contain as the active ingredient quinazoline derivs. represented by the following general formula (I) or pharmacol. acceptable salts thereof [wherein R5, R6, R7, R8 = H, substituents selected from a group of substituents A; or two adjacent groups of R5-R8 together represent methylenedioxy or CH:CHCH:CH; wherein substituents A = C1-4 alkyl, halo, OH, C1-4 alkoxy, C1-4 acyloxy, NR13R14 (R13, R14 = H, C1-4 alkyl), NHCOR15 (R15 = H, C1-4 alkyl), Ph, PhO, cyano, C1-4 acyl, CO2H, C2-5 alkoxycarbonyl, CONH2, N-(C1-4 alkyl)carbamoyl, N, N-di(C1-4 alkyl) carbamoyl; R2 = (un) substituted aryl or heteroaryl; n =0, 1; X = a group of the following general formula -P-NR9R10 or Q; wherein P = (un) branched C2-6 alkylene; R9, R10 = H, C1-4 alkyl, C2-4hydroxyalkyl, C3-6 alkoxyalkyl; Y = CHR11, O, S, NR12 (wherein R11 = H, C1-4 alkyl, OH, hydroxymethyl, methoxycarbonyl, ethoxycarbonyl; R12 = H, C1-4 alkyl, aryl optionally substituted by substituents A); Z = H or OH when Y = CHR11; Z = H when Y = O, S, or NR12]. Also disclosed are medicinal compns. containing I for preventing or treating autoimmune diseases or diseases caused by excessive production of TNF- α or IL-6. These compds. I inhibit the unusual production of TNF- α or IL-6 of macrophage or monocyte activated by bacterial DNA and are useful for treating or preventing diseases caused by unusual increase in cytokines, e.g. chronic articular rheumatism, systemic lupus erythematosus (SLE), septicemia, inflammatory bowel diseases, osteoarthritis, multiple sclerosis, Behcet's disease, rejection of bone marrow transplant, hepatitis, type II diabetes, atrial myxoma, alc. hepatic cirrhosis, myeloma, and mesangium-proliferative nephritis. Thus, mesylation of 4-(4-hydroxybutylamino)-6,7-dimethoxy-2-(2-naphthyl)quinazoline by methanesulfonyl chloride and Et3N in CH2Cl2 under ice-cooling for 1 h and at room temperature for 4 h followed by amination with N-(2-methoxyethyl) ethylamine at room temperature at room temperature for 2

days gave

6,7-dimethoxy-4-(4-(ethyl-(2-methoxyethyl)amino)butylamino)-2-(2-naphthyl)quinazoline (II). II in vitro inhibited the production of TNF- α in mouse spleen cells with IC50 of 10 nM and that of IL-6 with IC50 of 32 nM.

IT 445401-96-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel quinazoline derivs. for preventing or treating inflammatory diseases caused by bacterial DNA)

RN 445401-96-7 CAPLUS

CN 1,3-Propanediamine, N3-[6,7-dimethoxy-2-(4-pyridinyl)-4-quinazolinyl]- N1,N1-dimethyl- (CA INDEX NAME)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:504782 CAPLUS

DOCUMENT NUMBER: 137:78968

TITLE: Preparation of aminocarbonylpyrrolidine derivatives as

dipeptidyl peptidase IV inhibitors

INVENTOR(S): Matsuno, Kenji; Ueno, Kimihisa; Iwata, Yasuhiro;

Matsumoto, Yuichi; Nakanishi, Satoshi; Takasaki, Kotaro; Kusaka, Hideaki; Nomoto, Yuji; Ogawa, Akira

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 196 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA.	PATENT NO.					KIND DATE			APPLICATION NO.					DATE			
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EP	1354	882			A1		2003	1022		EP 2	001-	2718	92		2	0011	227 <
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OTHER SOURCE(S):

MARPAT 137:78968

AB Title compds. [I; Q = CH2, S; R = H, (S)-CN; B = CH2CO, COCH2, CO; YXW = NHCH2CH2NH, NH(CH2)3NH, NHCH2C(CH3)2NH,

1-(4-methyl-piperidine-4-amino)-yl, 1-(1-aminomethylcyclopropyl)amino,

4-NHCH2C6H4CH2NH, N(CH3)CH2CH2N(CH3), 1,4-piperazinyl,

1-piperidinyl-4-amino, N(CH3)CH2C(CH3)2NH; Z = optionally substituted

1-pyrrolidinyl, optionally substituted 3-thiazolidinyl, optionally substituted 1-oxo-3-thiozolidinyl, etc.] and pharmacol. acceptable salts of title compds. are prepared as dipeptidyl peptidase IV inhibitors. Title compds. are useful as antidiabetics, antiaids agents, antiarteriosclerosis, antihyperglycinemia agents, and as remedies for hyperglycinemia, hyperinsulinism, etc. in combination with related remedies as GI-262570, KAD1229, etc. Thus, the title compound II was prepared and in vivo tested for DPP-IV inhibition with IC50 = 11 nmol/L.

IT 440099-77-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminocarbonylpyrrolidine derivs. as dipeptidyl peptidase ${\tt IV}$ inhibitors)

RN 440099-77-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[2-[[2-[[2-(4-pyridinyl)-4-quinazolinyl]amino]ethyl]amino]acetyl]-, (2S)-, methanesulfonate (1:2) (CA INDEX NAME)

CM 1

CRN 440099-76-3 CMF C22 H23 N7 O

Absolute stereochemistry.

CM 2

CRN 75-75-2 CMF C H4 O3 S

IT 380588-03-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aminocarbonylpyrrolidine derivs. as dipeptidyl peptidase IV inhibitors)

RN 380588-03-4 CAPLUS

CN 1,2-Ethanediamine, N1-[2-(4-pyridinyl)-4-quinazolinyl]- (CA INDEX NAME)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220584 CAPLUS

DOCUMENT NUMBER: 136:247584

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease

INVENTOR(S): Bebbington, David; Knegtel, Ronald; Golec, Julian M.

C.; Li, Pan; Davies, Robert; Charrier, Jean-Damien

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 356 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PAT	TENT :	NO.			KIN	D	DATE			APF	LICA	TION	NO.		D	ATE		
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EP 1345922 B1 20060531

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A 20040430

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EP 1702920

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			AU 2006-201396	АЗ	20060404
OTHER SOURCE(S).	млррлт	136.247584			

(Uses)

AΒ Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un) substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)20, C(R6)2S0-2, C(R6)2NR6, C0, C02, CR6OCO, CR60CONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un) substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially

inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 = CR9; Z2 and Z3 = N; Z4 = CRy]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μ M for glycogen synthetase kinase 3 β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2.

IT 404828-10-0P, (5-Methyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)-amine 404828-11-1P, (7-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine 404828-12-2P, (6-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine 404828-45-1P, (2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P, (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-11-1 CAPLUS

CN 4-Quinazolinamine, 7-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-12-2 CAPLUS

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404828-50-8 CAPLUS
CN 4-Quinazolinamine, N-[5-(1,1-dimethylethyl)-1H-pyrazol-3-yl]-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220583 CAPLUS

DOCUMENT NUMBER: 136:247583

TITLE: Preparation of pyrazolamines and analogs as protein

kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease

INVENTOR(S): Davies, Robert; Bebbington, David; Knegtel, Ronald;

Wannamaker, Marion; Li, Pan; Forester, Cornelia;

Pierce, Albert; Kay, David

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 373 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

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ES 2266258

T3 20070301

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B1 20060531

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL
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ΑU	2006-201396	А3	20060404	

OTHER SOURCE(S):

MARPAT 136:247583

as

AΒ Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR60CONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un) substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially

inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRy; G = Ring C]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μ M for glycogen synthetase kinase 3 β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2.

IT 404828-10-0P, (5-Methyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)-amine 404828-11-1P, (7-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine

404828-12-2P, (6-Chloro-2-pyridin-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl) amine 404828-45-1P,

(2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P, (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-11-1 CAPLUS

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RN 404828-12-2 CAPLUS

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN $40\,48\,28\,-50\,-8$ CAPLUS

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220582 CAPLUS

DOCUMENT NUMBER: 136:247582

TITLE: Preparation of pyrazolamines and analogs as protein

kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease

INVENTOR(S): Bebbington, David; Binch, Hayley; Knegtel, Ronald;

Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert; Li, Pan;

Wannamaker, Marion; Forster, Cornelia; Pierce, Albert

wannamaker, narron, rorster, cornerra, rrerte

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 355 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

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ΑIJ	2006-201396	А3	20060404	

OTHER SOURCE(S):

MARPAT 136:247582

01

AΒ Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6) 2NR6CO, C(R6) 2NR6CO2, CR6:NNR6, CR6:NO, C(R6) 2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially

as

inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRy; G = Ring D]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μ M for glycogen synthetase kinase 3 β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2.

IT 404828-10-0P, (5-Methyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)-amine 404828-11-1P, (7-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine 404828-12-2P, (6-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine 404828-45-1P,

(2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P, (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-11-1 CAPLUS

CN 4-Quinazolinamine, 7-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-12-2 CAPLUS

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-50-8 CAPLUS

CN 4-Quinazolinamine, N-[5-(1,1-dimethylethyl)-1H-pyrazol-3-yl]-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220581 CAPLUS

DOCUMENT NUMBER: 136:247581

TITLE: Preparation of pyrazolamines and analogs as protein

kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease

INVENTOR(S): Golec, Julian M. C.; Charrier, Jean-Damien; Knegtel,

Ronald; Bebbington, David; Davies, Robert; Li, Pan

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

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MARPAT 136:247581

as

Ι

AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un) substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)20, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un) substituted aliphatic group; or N(R6)2 = heterocyclylor heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially

inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrazolamines and indazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N; at least one of Z1 or Z3 = N]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidiny1)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2.

404828-10-0P, (5-Methyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-y1)-amine 404828-11-1P, (7-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine 404828-12-2P, (6-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2Hpyrazol-3-yl)amine 404828-45-1P, (2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P , (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-11-1 CAPLUS

CN 4-Quinazolinamine, 7-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-12-2 CAPLUS

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-50-8 CAPLUS

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220580 CAPLUS

DOCUMENT NUMBER: 136:247606

TITLE: Preparation of 3-(4-pyrimidinylamino)pyrazole

derivatives as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treating cancer, diabetes

and Alzheimer's disease.

INVENTOR(S): Davies, Robert; Bebbington, David; Binch, Haley;

Knegtel, Ronald; Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

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OTHER SOURCE(S): GΙ

MARPAT 136:247606

AΒ The preparation of title compds. I and their pharmaceutically acceptable salts or prodrugs is described [wherein: R1, R2 = dependently form (un) substituted fused, unsatd. or partially unsatd., 5-8 membered carbocyclo ring; R3, R4 = independently H, aliphatic, aryl, heteroaryl, heterocyclyl, or wide variety of functionalized sidechains; or dependently form a fused, 5-8 membered, unsatd. or partially unsatd. ring having 0-3ring heteroatoms (N, S, O); R5 = fused, (un)substituted 5-7 membered monocyclic ring or 8-10 membered bicyclic ring (aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms (N, S, O))]. For example, chlorination of quinazolone II with phosphorus oxychloride, followed by condensation with 3-amino-5-methylpyrazole afforded claimed compound III. Compds. I are inhibitors of GSK-3 and Aurora-2 protein kinases. The invention also relates to methods of treating diseases associated with these protein kinases, such as diabetes, cancer and Alzheimer's disease. In bioassays, compds. I inhibited the following kinases with Kis reported < 100 nM: GSK-3 β (163 compds.), AURORA-2 (65 compds.), CDK-2 (no data), ERK2 (8 compds.), AKT (no data), and Human Src kinase (21 compds.). Claims included 146 specific compds., and 188 examples were given. The syntheses of 6 compds. and 46 intermediates are described.

ΙT 404828-10-0P 404828-11-1P 404828-12-2P

404828-45-1P 404828-50-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-(4-pyrimidinylamino)pyrazole compds. as protein kinase inhibitors)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

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RN 404828-11-1 CAPLUS

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REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220579 CAPLUS

DOCUMENT NUMBER: 136:247580

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease

INVENTOR(S): Davies, Robert; Li, Pan; Golec, Julian; Bebbington,

David

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 406 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

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MARPAT 136:247580

as

Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted AB Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)20, C(R6)2S0-2, C(R6)2NR6, C0, C02, CR6OCO, CR60CONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un) substituted aliphatic group; or N(R6)2 = heterocyclylor heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially

inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (triazinyl)pyrazolamines and indazolamines I [wherein Z1, Z2, and Z3 = N; Z4 = CRy]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3 β (GSK-3 β) and

 $0.1-1.0~\mu\text{M}$ for Aurora-2.

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(2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P, (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

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REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220578 CAPLUS

DOCUMENT NUMBER: 136:263164

TITLE: Preparation of triazolamines as protein kinase

inhibitors for treatment of cancer, diabetes, and

Alzheimer's disease

INVENTOR(S): Bebbington, David; Knegtel, Ronald; Binch, Haley;

Golec, Julian M. C.; Li, Pan; Charrier, Jean-Damien

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 377 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

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			US 2003-624800	A3 20030722 <

MARPAT 136:263164

GΙ

OTHER SOURCE(S):

AΒ Triazolamines I and pyrazolamines II [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T =a bond or alkylidene chain; W = C(R6)20, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR60CO, CR60CONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6) 2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substituted aliphatic, (hetero) aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un) substituted aliphatic group; or N(R6)2 =heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 =R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (heterocyclyl)triazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; R9 is defined above]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-quinazoliny1)-1H-1,2,4-triazol-3-amine III was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3 β) and 1.0-20 μ M for Aurora-2.

404828-10-0P, (5-Methyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-ΤТ 4-yl)-amine 404828-11-1P, (7-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine 404828-12-2P, (6-Chloro-2-pyridin-4-ylquinazolin-4-yl)(5-methyl-2Hpyrazol-3-yl)amine 404828-45-1P, (2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P , (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404891-18-5P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (protein kinase inhibitor; preparation of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404828-11-1 CAPLUS

CN 4-Quinazolinamine, 7-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-12-2 CAPLUS

CN 4-Quinazolinamine, 6-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-45-1 CAPLUS

CN 4-Quinazolinamine, N-1H-pyrazol-3-yl-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-50-8 CAPLUS

CN 4-Quinazolinamine, N-[5-(1,1-dimethylethyl)-1H-pyrazol-3-yl]-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404891-18-5 CAPLUS

CN 4-Quinazolinamine, N-(3-methyl-1H-1,2,4-triazol-5-yl)-2-(4-pyridinyl)-

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220577 CAPLUS

DOCUMENT NUMBER: 136:247579

TITLE: Preparation of pyrazolamines and analogs as protein

kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease

INVENTOR(S): Knegtel, Ronald; Bebbington, David; Binch, Hayley;

Golec, Julian; Patel, Sanjay; Charrier, Jean-Damien;

Kay, David; Davies, Robert; Li, Pan; Wannamaker,

Marion; Forster, Cornelia; Pierce, Albert

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA SOURCE: PCT Int. Appl., 376 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

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OTHER SOURCE(S):

MARPAT 136:247579

AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SOO-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR,

NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially

inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrimidinyl- and pyridinyl- pyrazolamines and indazolamines I [wherein Z1 = N, CRa, or CH; Z2 = N or CH; and at least one of Z1 or Z2 = N; Z3 = CRx; Z4 = CRy; Ra = halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, etc.; R and R4 are defined above]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μ M for glycogen synthetase kinase 3 β

(GSK-3 β) and 0.1-1.0 μ M for Aurora-2. IT 404828-10-0P, (5-Methyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)-amine 404828-11-1P,

(7-Chloro-2-pyridin-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl) amine 404828-12-2P, (6-Chloro-2-pyridin-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl) amine 404828-45-1P,

(2H-Pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine 404828-50-8P, (5-tert-Butyl-2H-pyrazol-3-yl)(2-pyridin-4-ylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404828-10-0 CAPLUS

CN 4-Quinazolinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-11-1 CAPLUS

CN 4-Quinazolinamine, 7-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-12-2 CAPLUS

CN 4-Quinazolinamine, 6-chloro-N-(5-methyl-1H-pyrazol-3-yl)-2-(4-pyridinyl)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-45-1 CAPLUS

CN 4-Quinazolinamine, N-1H-pyrazol-3-yl-2-(4-pyridinyl)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404828-50-8 CAPLUS

CN 4-Quinazolinamine, N-[5-(1,1-dimethylethyl)-1H-pyrazol-3-yl]-2-(4-dimethylethyl)

pyridinyl) - (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

2002:158388 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 136:200203

TITLE: Preparation of 4-aminoquinazolines for use in

inhibiting neoplastic cells and related conditions

INVENTOR(S): Pamukcu, Rifat; Piazza, Gary

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont. of U.S. Ser. No.

60,444, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

GΙ

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020025968	A1	20020228	US 2001-952769	20010914 <
PRIORITY APPLN. INFO.:			US 1998-60444 B1	19980415 <
OTHER SOURCE(S):	MARPAT	136:200203		

$$(R^4)_n$$
 N
 A
 $Z-CyB-(R^3)_m$

HC
$$\equiv$$
 C N N II

AB Title compds. I [wherein R1 = H or alkyl; Y = alkylene; A = ORa or S(O)pRa; Ra = alkylhydroxy; p = 0-2; Z = single bond, methylene, ethylene, vinylene, or ethynylene; CyB = heterocyclic ring; R3 = H, alkyl, alkoxy, halo, or CF3; R4 = H, alkyl, alkoxy, CO2H, carboxy ester, alkanoylamino, alkylsulfonylamino, alkylthio, alkylsulfinyl, alkylsulfonyl, ethynyl, hydroxymethyl, acetyl, or (un)substituted sulfamoyl, carbamoyl, etc.; m and n = independently 1-2; or pharmaceutically acceptable salts or hydrates thereof] were prepared for inhibiting neoplastic cells and related conditions. For example, amination of 2,4-dichloro-6-(2-triethylsilylethynyl)quinazolin-2,4-dione (preparation given) with 2-methoxyethylamine in CHC13, followed by addition of imidazole in EtOH and deprotection using NBu4F, afforded II. I are useful in the treatment of precancerous and cancerous lesions, including malignant melanomas, breast cancer, and colon cancer (no data).

IT 1102370-13-7

RL: PRPH (Prophetic)

(Preparation of 4-aminoquinazolines for use in inhibiting neoplastic cells and related conditions)

RN 1102370-13-7 CAPLUS

CN 4-Quinazolinamine, N-methyl-N-phenyl-2-(4-pyridinyl)-, hydrochloride (1:2) (CA INDEX NAME)

●2 HC1

ACCESSION NUMBER: 2000:161275 CAPLUS

DOCUMENT NUMBER: 132:194387

TITLE: Preparation of quinazolines as $p38-\alpha$ kinase and

TGF- β inhibitors

INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Perumattam,

John J.; Schreiner, George F.; Liu, David Y.; Lewicki,

John A.

PATENT ASSIGNEE(S): Scios Inc., USA

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PATENT NO.									APPLICATION NO.					DATE			
WO	WO 2000012497 WO 2000012497				A2	A2 20000309								19990827 <			<	
	W:	PL,	IS, RO,	JP, SG,	KP,	KR, SK,	LC,	BR, LK, TT,	LR,	LT,	LV,	MG,	MK,	MN,	MX,	NO,	NΖ,	
		GH, ES, CI,	GM, FI, CM,	KE, FR, GA,	LS, GB, GN,	MW, GR, GW,	IE, ML,	IT, MR,	LU, NE,	MC, SN,	NL, TD,	PT, TG	SE,	BF,	BJ,	CF,	CG,	
US	6184	226			В1		2001	0206		US 1	998-	1419	16		1	9980	828	
	2342																	
	9962							0321		AU 1	999-	6241.	3		1	9990	827	<
	7719																	
	1107									EP 1	999-	9495	68		1	9990	827	<
EP	1107						2006	-										
	R:	ΑT,								GR,	ΙΤ,	LI,	LU,	ΝL,	SE,	MC,	PT,	
		IE,	SI,	LT,	LV,	FI,	RO,	CY										
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JP	2002 1152	5235	02		${ m T}$		2002	0730		JP 2								
					С					CN 1						9990		-
	3422				Т			1115		AT 1						9990		
	2274							0516		ES 1						9990		
	2001									MX 2								
	1035				A1		2007	0601		HK 2						0010		
PRIORITY	Y APP	LN.	INFO	.:						US 1 WO 1					A 1 W 1			

OTHER SOURCE(S):

GΙ

AB Title compds. [I; R = ZR1; R1 = (un)substituted cyclic (hetero)aliphatic group, -(hetero)aryl; R3 = noninterfering substituent (sic); R4R5 = atoms to complete a 6-membered aromatic ring containing 0, 1, or 2 nonadjacent N atoms

MARPAT 132:194387

and noninterfering substituent(s) (sic); z = bond or linker (sic); Z3 = CR2 or N; R2 = noninterfering substituent (sic)] were prepared Thus, prepn

of, e.g., 4-(4-pyridinylamino)-2-phenylquinazoline was described. Data for biol. activity of I were given.

IT 474289-44-6

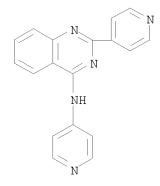
RL: PRPH (Prophetic)

(Preparation of quinazolines as p38- α kinase and TGF- β

inhibitors)

RN 474289-44-6 CAPLUS

CN 4-Quinazolinamine, N,2-di-4-pyridinyl- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:795361 CAPLUS

DOCUMENT NUMBER: 124:29779

ORIGINAL REFERENCE NO.: 124:5715a,5718a

TITLE: 4-Aminoquinazoline derivatives as inhibitors of cGMP

phosphodiesterase and TXA2 synthetase

INVENTOR(S): Lee, Sung J.; Konishi, Yoshitaka; Macina, Orest T.;

Kondo, Kigen; Yu, Dingwei T.

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: U.S., 42 pp. Cont.-in-part of U.S. Ser. No. 76,431,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	API	PLICATION NO.		DATE	
						_		
	US 5439895	A	19950808	US	1993-154691		19931119 <	
	JP 06192235	A	19940712	JP	1993-197039		19930714 <	
	CA 2100626	A1	19940116	CA	1993-2100626		19930715 <	
	KR 191416	B1	19990615	KR	1993-13549		19930715 <	
	AT 208771	T	20011115	ΑT	1993-305557		19930715 <	
	ES 2167325	Т3	20020516	ES	1993-305557		19930715 <	
	JP 08099962	A	19960416	JP	1995-264667		19950920 <	
	JP 2923742	B2	19990726					
PRIOR	RITY APPLN. INFO.:			US	1992-913473	В2	19920715 <	
				US	1993-76431	В2	19930614 <	

OTHER SOURCE(S): MARPAT 124:29779

GΙ

$$(R^4)_n$$
 N
 $Z-CyB-(R^3)_m$

AB The compds. of the formula I and acid addition salts thereof, salts thereof, and hydrates thereof wherein R1 is hydrogen or C1-4 alkyl; Y is C1-6 alkylene; A is ORO or S(O)pRO, in which RO is C1-4 alkyl-hydroxy; p is 0-2; Z is single bond, methylene, ethylene, vinylene or ethynylene; CyB is (1) 7-membered, unsatd. or partially saturated, monocyclic hetero ring containing

II

as hetero atoms, one, two or three nitrogen atoms, (2) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms, two or

three nitrogen atoms, (3) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atom, one nitrogen atom, (4) 4- or 5-membered, unsatd. or partially saturated, monocyclic hetero ring containing

hetero atoms, one, two or three nitrogen atoms, or (5) 4-7 membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

one or two oxygen atoms, or one or two sulfur atoms; R3 = e.g., H, C1-4 alkyl, C1-4 alkoxy; R4 = e.g., H, C1-4 alkyl, C1-4 alkoxy; and m and n independently are 1 or 2; with the proviso that (1) a CyB ring does not bond to Z through a nitrogen atom in the CyB ring when Z is vinylene or ethynylene, have inhibitory effect on cGMP-PDE, and addnl. on TXA2 synthetase. Thus, e.g., $2-(1-\text{imidazolyl})-4-[2-(2-\text{hydroxyethoxy})\text{ethyl}]\text{amino-6-ethynylquinazoline.2HCl (II.2HCl) (prepared by$

desilylation of a silylacetylene precursor) exhibited inhibitory effect on cGMP-PDE and TXA2 synthetase with IC50 = 4.6 + 10-8 M and 1.33

+ 10-6 M, resp. Pharmaceutical formulations were given.

IT 157862-97-0P 157862-98-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(4-aminoquinazoline derivs. as inhibitors of cGMP phosphodiesterase and TXA2 synthetase)

RN 157862-97-0 CAPLUS

as

CN 4-Quinazolinamine, N-(phenylmethyl)-2-(4-pyridinyl)- (CA INDEX NAME)

RN 157862-98-1 CAPLUS

CN 4-Quinazolinamine, N-(phenylmethyl)-2-(4-pyridinyl)-, hydrochloride (1:2) (CA INDEX NAME)

●2 HC1

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:761961 CAPLUS

DOCUMENT NUMBER: 123:340173

ORIGINAL REFERENCE NO.: 123:61059a,61062a

TITLE: 4-Aminoquinazoline derivatives as inhibitors of cyclic

guanosine 3',5'-monophosphate phosphodiesterase and

thromboxane A2 synthetase

INVENTOR(S): Lee, Sung J.; Konishi, Yoshitaka; Macina, Orest T.;

Kondo, Kigen; Yu, Dingwei T.

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: U.S., 44 pp. Cont.-in-part of U.S. Ser. No. 76,431,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5436233	A	19950725	US 1993-154518	19931119 <
JP 06192235	A	19940712	JP 1993-197039	19930714 <
CA 2100626	A1	19940116	CA 1993-2100626	19930715 <
KR 191416	В1	19990615	KR 1993-13549	19930715 <
AT 208771	T	20011115	AT 1993-305557	19930715 <
ES 2167325	Т3	20020516	ES 1993-305557	19930715 <
JP 08099962	A	19960416	JP 1995-264667	19950920 <
JP 2923742	B2	19990726		
PRIORITY APPLN. INFO.:			US 1992-913473	B2 19920715 <
			US 1993-76431	B2 19930614 <
	~- ~	~- 400 04045	0	

OTHER SOURCE(S): CASREACT 123:340173; MARPAT 123:340173

GΙ

$$(R^4)_n$$
 N
 $Z-CyB-(R^3)_m$
 I

AB Title compds. I [R1 is H, C1-4 alkyl; Y is a single bond or C1-6 alkylene; A is (i) CyA-(R2)1, (ii) ORO or S(O)pRO in which RO is ROA or ROB; ROA is CyA-(R2)1; ROB is H or C1-4 alkyl; p is 0-2; CyA is, e.g., (1) 3-7 membered, saturated or unsatd., monocyclic carbocyclic ring, (2) 7-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

one nitrogen atom, one nitrogen and one oxygen atoms, two nitrogen and one oxygen atoms, or one nitrogen and two oxygen atoms, (3) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

one nitrogen and one oxygen atoms, two nitrogen and one oxygen atoms, or one nitrogen and two oxygen atoms; R2 is R2A or R2B; R2A is, e.g., CF3, OCF3; R2B is, e.g., H, C1-4 alkyl, C1-4 alkoxy; Z is ZA or ZB, ZA is methylene, ethylene, ethynylene; ZB is a single bond; CyB is, e.g., (1) 7-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms, one, two or three nitrogen atoms, (2) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as hetero atoms,

two or three nitrogen atoms, (3) 6-membered, unsatd. or partially saturated, monocyclic hetero ring containing as a hetero atom, one nitrogen atom; R3 = e.g., H, C1-4 alkyl; R4 = e.g., NHSO2R11, R11 = e.g., C1-4 alkyl; l, m, n are independently 1 or 2 (with provisos)] are provided as inhibitors of cGMP-PDE and TXA2 synthetase. Thus, e.g., treatment of 2-(1-imidazolyl)-4-(2-methoxyethyl) amino-6-(2-triethylsilylethynyl) quinazoline (preparation given) with tetrabutylammonium fluoride afforded 6-ethynyl-4-(2-methoxyethyl) amino-2-(1-imidazolyl) quinazoline (II); II.2HCl demonstrated inhibition of cGMP-PDE with and TXA2 synthetase with IC50 = 4.6+10-8 and 2.4+10-6 M, resp. Pharmaceutical formulations were given. 157862-97-0P

IT 157862-97-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(4-aminoquinazoline derivs. as inhibitors of cyclic guanosine 3',5'-monophosphate phosphodiesterase and thromboxane A2 synthetase) 157862-97-0 CAPLUS

CN 4-Quinazolinamine, N-(phenylmethyl)-2-(4-pyridinyl)- (CA INDEX NAME)

RN

IT 157862-98-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
 (4-aminoquinazoline derivs. as inhibitors of cyclic guanosine
 3',5'-monophosphate phosphodiesterase and thromboxane A2 synthetase)
157862-98-1 CAPLUS
4-Quinazolinamine, N-(phenylmethyl)-2-(4-pyridinyl)-, hydrochloride (1:2)

(CA INDEX NAME)

RN

CN

●2 HC1

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:605373 CAPLUS

DOCUMENT NUMBER: 121:205373

ORIGINAL REFERENCE NO.: 121:37397a,37400a

TITLE: 4-aminoquinazoline derivatives, and their use as

medicine

INVENTOR(S): Lee, Sung Jai; Konishi, Yoshitaka; Macina, Orest

Taras; Kondo, Kigen; Yu, Dingwei Tim

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 86 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 579496 EP 579496	A1 B1	19940119 20011114	EP 1993-305557	19930715 <
R: AT, BE, CH,			GB, GR, IE, IT, LI,	LU, MC, NL, PT, SE
JP 06192235	A	19940712	JP 1993-197039	19930714 <
CA 2100626	A1	19940116	CA 1993-2100626	19930715 <
KR 191416	В1	19990615	KR 1993-13549	19930715 <
AT 208771	T	20011115	AT 1993-305557	19930715 <
ES 2167325	Т3	20020516	ES 1993-305557	19930715 <
JP 08099962	A	19960416	JP 1995-264667	19950920 <
JP 2923742	В2	19990726		
PRIORITY APPLN. INFO.:			US 1992-913473	A 19920715 <
			US 1993-76431	A 19930614 <
OTHER SOURCE(S):	MARPAT	121:20537	3	

OTHER SOURCE(S): MARPAT 121:205373

GΙ

AB The title compds. I wherein R1 is H or alkyl; Y is bond or alkylene; A is (i) -CyAR2, (ii) -OR0 or -S(O)pR0, R0 = H, alkyl, etc., p is 0-2, (iii) -NR16R17, R16, R17 are H, alkyl; CyA is (1) a 3-7 membered monocyclic carbocyclic ring, (2) a 4-7 membered monocyclic hetero ring containing as hetero atoms, one N atom, one N and one O atoms, two N and one O atoms, or one N and two O atoms, (3) a 4-7 membered monocyclic hetero ring containing as hetero atoms, 1 or 2 O or S atoms, R2 is (1) H, (2) alkyl, (3) alkoxy, (4) -COOR5, in which R5 is H or alkyl, (5) -NR6R7, R6, R7 are H, alkyl, (6) -SO2NR6R7, (7) halogen, (8) CF3, (9) NO2 or (10) CF3O; Z is bond, methylene, ethylene, vinylene or ethynylene; CyB is a heterocyclic ring; R3 is H, alkyl, alkoxy, halogen or CF3; R4 is H, alkyl, alkoxy, etc., and acid addition salts thereof, salts thereof, and hydrates thereof were prepared and have inhibitory effect on cGMP-PDE, or addnl. on TXA2 synthetase. Thus, a representative prepared compound II had inhibitory activity IC50 of 3.6 x 10-7 on cGMP-PDE.

IT 157862-97-0P 157862-98-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as cardiovascular agents)

RN 157862-97-0 CAPLUS

CN 4-Quinazolinamine, N-(phenylmethyl)-2-(4-pyridinyl)- (CA INDEX NAME)

RN 157862-98-1 CAPLUS

CN 4-Quinazolinamine, N-(phenylmethyl)-2-(4-pyridinyl)-, hydrochloride (1:2) (CA INDEX NAME)

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COST IN U.S. DOLLARS
FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION
-17.22
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SINCE FILE TOTAL ENTRY SESSION

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121.68

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=> Y

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LOGOFF? (Y)/N/HOLD:Y

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PASSWORD:

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^ ^ ^	^ ^	^ ^	^ ^	* Welcome to STN International * * * * * * * * * *
NEWS	1			Web Page for STN Seminar Schedule - N. America
NEWS	2	DEC	01	ChemPort single article sales feature unavailable
NEWS	3	JAN		The retention policy for unread STNmail messages
				will change in 2009 for STN-Columbus and STN-Tokyo
NEWS	4	JAN	07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
				Classification Data
NEWS	5	FEB	02	Simultaneous left and right truncation (SLART) added
	_			for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS	6	FEB		GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS	7	FEB		Patent sequence location (PSL) data added to USGENE COMPENDEX reloaded and enhanced
NEWS NEWS	8 9	FEB FEB		WTEXTILES reloaded and enhanced
NEWS	-	FEB		New patent-examiner citations in 300,000 CA/CAplus
MEMP	10	r ED	19	patent records provide insights into related prior
				art
NEWS	11	FEB	19	Increase the precision of your patent queries use
				terms from the IPC Thesaurus, Version 2009.01
NEWS	12	FEB	23	Several formats for image display and print options
				discontinued in USPATFULL and USPAT2
NEWS	13	FEB	23	MEDLINE now offers more precise author group fields
				and 2009 MeSH terms
NEWS	14	FEB	23	TOXCENTER updates mirror those of MEDLINE - more
	4.5		0.0	precise author group fields and 2009 MeSH terms
NEWS	15	FEB	23	Three million new patent records blast AEROSPACE into
NEWS	16	FEB	2 5	STN patent clusters
NEWS	ΤО	FEB	25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS	17	MAR	06	INPADOCDB and INPAFAMDB enhanced with new display
MEMO	Τ,	111111	00	formats
NEWS	18	MAR	11	EPFULL backfile enhanced with additional full-text
_				applications and grants
NEWS	19	MAR	11	ESBIOBASE reloaded and enhanced
NEWS	20	MAR	20	CAS databases on STN enhanced with new super role
				for nanomaterial substances
NEWS	21	MAR	23	CA/CAplus enhanced with more than 250,000 patent
				equivalents from China
NEWS		MAR		IMSPATENTS reloaded and enhanced
NEWS	23	APR	03	CAS coverage of exemplified prophetic substances
MEMC	2.4	7 DD	0.7	enhanced
NEWS NEWS		APR APR		STN is raising the limits on saved answers CA/CAplus now has more comprehensive patent assignee
MEMP	23	ALI	4	information
NEWS	26	APR	26	USPATFULL and USPAT2 enhanced with patent
				assignment/reassignment information
NEWS	27	APR	28	CAS patent authority coverage expanded
NEWS	28	APR	28	ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS	29	APR	28	Limits doubled for structure searching in CAS
				REGISTRY

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FULL ESTIMATED COST

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STRUCTURE FILE UPDATES: 26 APR 2009 HIGHEST RN 1139453-56-7 DICTIONARY FILE UPDATES: 26 APR 2009 HIGHEST RN 1139453-56-7

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http://www.cas.org/support/stngen/stndoc/properties.html

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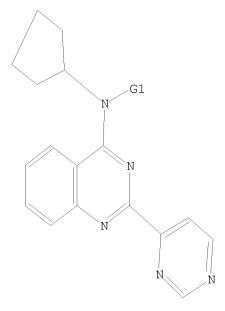
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chain nodes :
19
ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17 21 22 23 24 25
ring/chain nodes :
18
chain bonds :
7-18 9-12 18-19 18-21
ring bonds :
1-2 \quad 1-6 \quad 2-3 \quad 3-4 \quad 4-5 \quad 5-6 \quad 5-7 \quad 6-10 \quad 7-8 \quad 8-9 \quad 9-10 \quad 12-13 \quad 12-17 \quad 13-14 \quad 14-15
15-16 16-17 21-22 21-25 22-23 23-24 24-25
exact/norm bonds :
7-18 18-19 18-21 21-22 21-25 22-23 23-24 24-25
exact bonds :
9-12
normalized bonds :
1-2 \quad 1-6 \quad 2-3 \quad 3-4 \quad 4-5 \quad 5-6 \quad 5-7 \quad 6-10 \quad 7-8 \quad 8-9 \quad 9-10 \quad 12-13 \quad 12-17 \quad 13-14 \quad 14-15
15-16 16-17
isolated ring systems :
containing 1 : 12 :
```

G1:Hy,Ak

Match level: 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom

L1 STRUCTURE UPLOADED

=> d 11L1 HAS NO ANSWERS L1STR



G1 Hy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 15:28:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 5 TO 234

PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 15:28:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 169 TO ITERATE

100.0% PROCESSED 169 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=>

Uploading C:\Program Files\STNEXP\Queries\10552426newpyrim.str

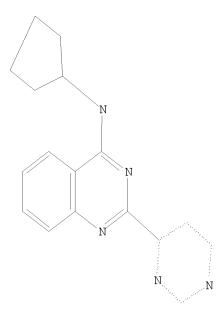
ring nodes : $1 \quad \overset{.}{2} \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \quad 8 \quad 9 \quad 10 \quad 12 \quad 13 \quad 14 \quad 15 \quad 16 \quad 17 \quad 19 \quad 20 \quad 21 \quad 22 \quad 23$ ring/chain nodes : 18 chain bonds : 7-18 9-12 18-19 ring bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 12-13 12-17 13-14 14-15 15-16 16-17 19-20 19-23 20-21 21-22 22-23 exact/norm bonds : 7-18 12-13 12-17 13-14 14-15 15-16 16-17 18-19 19-20 19-23 20-21 21-22 22-23 exact bonds : 9-12 normalized bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 isolated ring systems : containing 1 : 12 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom

L4 STRUCTURE UPLOADED

=> d 14 L4 HAS NO ANSWERS L4 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 14

SAMPLE SEARCH INITIATED 15:30:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 5 TO 234 PROJECTED ANSWERS: 0 TO 0

L5 0 SEA SSS SAM L4

=> s 14 sss full

FULL SEARCH INITIATED 15:30:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 169 TO ITERATE

100.0% PROCESSED 169 ITERATIONS 2 ANSWERS

SEARCH TIME: 00.00.01

L6 2 SEA SSS FUL L4

=> d scan

L6 2 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 1H-Inden-2-ol, 2,3-dihydro-1-[[2-[2-(methylthio)-4-pyrimidinyl]-4-quinazolinyl]amino]-, <math>(1S,2R)-

MF C22 H19 N5 O S

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 2 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 1H-Inden-2-ol, 1-[[2-(2-amino-4-pyrimidinyl)-4-quinazolinyl]amino]-2,3-(12.07)

dihydro-, (1S,2R)-MF C21 H18 N6 O

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=>

Uploading C:\Program Files\STNEXP\Queries\10552426meta.str

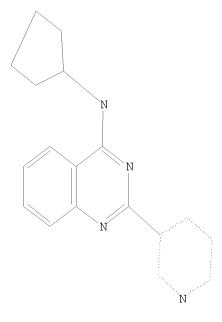
ring nodes : $1 \quad \overset{.}{2} \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \quad 8 \quad 9 \quad 10 \quad 12 \quad 13 \quad 14 \quad 15 \quad 16 \quad 17 \quad 19 \quad 20 \quad 21 \quad 22 \quad 23$ ring/chain nodes : 18 chain bonds : 7-18 9-12 18-19 ring bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 12-13 12-17 13-14 14-15 15-16 16-17 19-20 19-23 20-21 21-22 22-23 exact/norm bonds : 7-18 12-13 12-17 13-14 14-15 15-16 16-17 18-19 19-20 19-23 20-21 21-22 22-23 exact bonds : 9-12 normalized bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 isolated ring systems : containing 1 : 12 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom

L7 STRUCTURE UPLOADED

=> d 17 L7 HAS NO ANSWERS L7 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 17

SAMPLE SEARCH INITIATED 15:32:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

L8 0 SEA SSS SAM L7

=> s 17 sss full

FULL SEARCH INITIATED 15:33:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 312 TO ITERATE

100.0% PROCESSED 312 ITERATIONS 9 ANSWERS

SEARCH TIME: 00.00.01

L9 9 SEA SSS FUL L7

=> d scan

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 4-Quinazolinamine, N-cyclopentyl-2-(3-pyridinyl)-

MF C18 H18 N4

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):8

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 4-Quinazolinamine, N-(2,3-dihydro-1H-inden-1-yl)-2-(3-pyridinyl)-

MF C22 H18 N4

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 1H-Inden-2-ol, 1-[[2-(4-amino-3-pyridinyl)-4-quinazolinyl]amino]-2,3-dihydro-, <math>(1S,2R)-

MF C22 H19 N5 O

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Cyclopentanol, 2-[[2-(3-pyridinyl)-4-quinazolinyl]amino]-, (1R,2R)MF C18 H18 N4 O

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN 1H-Inden-2-ol, 2,3-dihydro-1-[[2-(3-pyridinyl)-4-quinazolinyl]amino]-,
(1S,2R)MF C22 H18 N4 O

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 4-Quinazolinamine, N-cyclopentyl-6,7-dimethoxy-2-(3-pyridinyl)-

MF C20 H22 N4 O2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 2(1H)-Pyridinone, 5-[4-[[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]amino]-2-quinazolinyl]-

MF C22 H18 N4 O2

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 1H-Inden-2-ol, 2,3-dihydro-1-[[2-(6-methoxy-3-pyridinyl)-7-

(trifluoromethyl)-4-quinazolinyl]amino]-, (1S,2R)-

MF C24 H19 F3 N4 O2

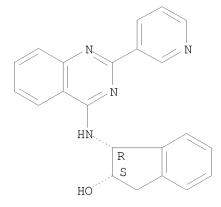
Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 9 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN 1H-Inden-2-ol, 2,3-dihydro-1-[[2-(3-pyridinyl)-4-quinazolinyl]amino]-, (1R,2S)-

MF C22 H18 N4 O



ALL ANSWERS HAVE BEEN SCANNED

=> fil cap
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 560.52 560.74

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FILE COVERS 1907 - 28 Apr 2009 VOL 150 ISS 18 FILE LAST UPDATED: 27 Apr 2009 (20090427/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

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=> s 19 L10 1 L9

=> d ibib abs

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:902403 CAPLUS

DOCUMENT NUMBER: 141:374752

TITLE: Heterocyclic compound modulators of kinases,

particularly Tie-2 kinase, and use in the treatment of

kinase-dependent diseases

INVENTOR(S): Ibrahim, Mohamed; Leahy, James; Sangalang, Joan C.;

Schnepp, Kevin; Shi, Xian; Nuss, John

PATENT ASSIGNEE(S): Exelixis, Inc., USA SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIND DATE				APPLICATION NO.						DATE				
	2004092196 2004092196									WO 2004-US10858					2	0040	408		
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OTHER SOURCE(S): MARPAT 141:374752

AB The invention provides compds. for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. Compds. of the invention inhibit, regulate and/or modulate kinases, particularly Tie-2. Methods of using the compds. and pharmaceutical compns. thereof to treat kinase-dependent diseases and conditions are also an aspect of the invention. Preparation of quinazoline compds. of the invention is described.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 16

L11 1 L6

=> d ibib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:902403 CAPLUS

DOCUMENT NUMBER: 141:374752

TITLE: Heterocyclic compound modulators of kinases,

particularly Tie-2 kinase, and use in the treatment of

kinase-dependent diseases

Ibrahim, Mohamed; Leahy, James; Sangalang, Joan C.; INVENTOR(S):

Schnepp, Kevin; Shi, Xian; Nuss, John

PATENT ASSIGNEE(S): Exelixis, Inc., USA SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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OTHER SOURCE(S): MARPAT 141:374752

The invention provides compds. for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. Compds. of the invention inhibit, regulate and/or modulate kinases, particularly Tie-2. Methods of using the compds. and pharmaceutical compns. thereof to treat kinase-dependent diseases and conditions are also an aspect of the invention. Preparation of quinazoline compds. of the invention is described.

REFERENCE COUNT:

FULL ESTIMATED COST

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ENTRY

TOTAL

SESSION

567.24

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